EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	WO-2005121102-$.did.	US-PGPUB; USPAT; DERWENT	OR	ON	2007/08/14 08:13
L2	1	WO-2005118554-$.did.	US-PGPUB; USPAT; DERWENT	OR	ON	2007/08/14 07:56
L3	2	"6867200".pn.	US-PGPUB; USPAT; DERWENT	OR	ON	2007/08/14 07:56
L4	0	WO-2000035886-$.did.	US-PGPUB; USPAT; DERWENT	OR	ON	2007/08/14 08:14
L5	1	WO-200035886-$.did.	US-PGPUB; USPAT; DERWENT	OR	ON	2007/08/14 08:58
L6	4	"537115".ap.	US-PGPUB; USPAT; DERWENT	OR	ON	2007/08/14 09:04
L7	439	548/309.7.ccls.	US-PGPUB; USPAT; DERWENT	OR	ON	2007/08/14 09:04
L8	197	548/310.7.ccls.	US-PGPUB; USPAT; DERWENT	OR	ON	2007/08/14 09:04
L9	21	l7 and l8	US-PGPUB; USPAT; DERWENT	OR	ON	2007/08/14 09:04
L10	1316	514/394.ccls.	US-PGPUB; USPAT; DERWENT	OR	ON	2007/08/14 09:05
L11	10	l10 and l9	US-PGPUB; USPAT; DERWENT	OR	ON	2007/08/14 09:05

factor VII a, IXa
Xa, XIa AXYS 19/33 current app. ED 12/03/03
pharmaceutical EFD 12/03/02
60/—

10/537,115A Yong Chu 08-13-2007

$%^STN;HighlightOn=;HighlightOff=;

22/33 ~~DDP/10ie~~ Not

Connecting via Winsock to STN

32/33 1026/1030/ODP

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LOGINID:ssptaylc1626

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	53.64	226.40

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CA SUBSCRIBER PRICE	-7.80	-7.80

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DICTIONARY FILE UPDATES: 12 AUG 2007 HIGHEST RN 944447-30-7

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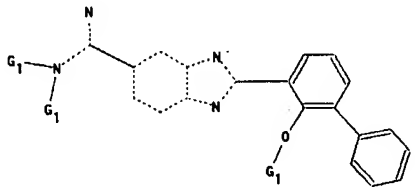

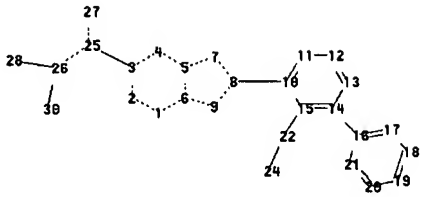

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ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
chain bonds :
3-25 8-10 14-16 15-22 22-24 25-26 25-27 26-28 26-30
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 10-11 10-15 11-12 12-13 13-14
14-15 16-17 16-21 17-18 18-19 19-20 20-21
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 15-22 22-24 25-26 25-27 26-28
26-30
exact bonds :
3-25 8-10 14-16
normalized bonds :
10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21 17-18 18-19 19-20 20-21

G1:H,CH3,CH2,Et,n-Pr,n-Bu

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom
22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 30:CLASS

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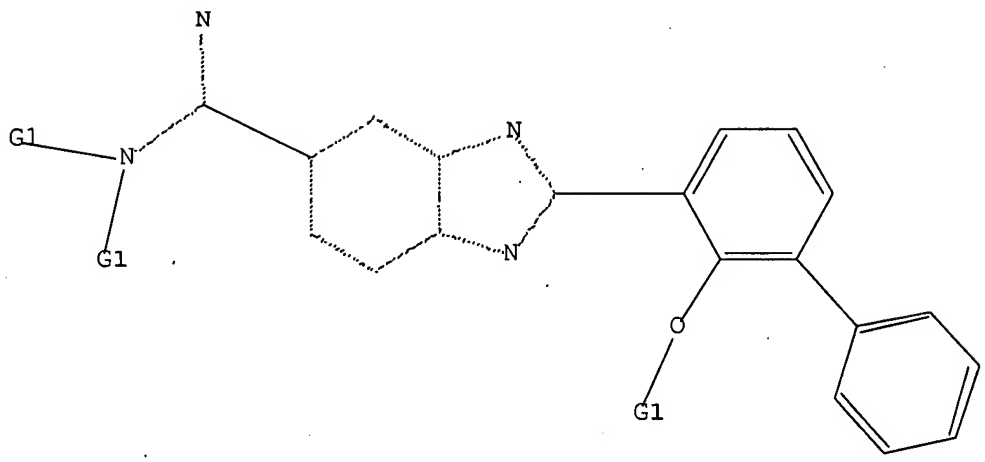
L5 STR



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Structure attributes must be viewed using STN Express query preparation.

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100.0% PROCESSED       31 ITERATIONS                          14 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          286 TO      954
PROJECTED ANSWERS:              56 TO      504

L6            14 SEA SSS SAM L5

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100.0% PROCESSED      592 ITERATIONS                         342 ANSWERS
SEARCH TIME: 00.00.01

L7           342 SEA SSS FUL L5

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COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              172.10     398.50

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                0.00      -7.80

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FILE COVERS 1907 - 13 Aug 2007 VOL 147 ISS 8
FILE LAST UPDATED: 12 Aug 2007 (20070812/ED)

=> s l7
L8 33 L7

=> d ibib abs tot

L8 ANSWER 1 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:757667 CAPLUS Full-text
DOCUMENT NUMBER: 145:305633
TITLE: Potent 4-amino-5-azaindole factor VIIa inhibitors
AUTHOR(S): Hu, Huiyong; Kolesnikov, Aleksandr; Riggs, Jennifer R.; Wesson, Kieron E.; Stephens, Robin; Leahy, Ellen M.; Shrader, William D.; Sprengeler, Paul A.; Green, Michael J.; Sanford, Ellen; Nguyen, Margaret; Gjerstad, Erik; Cabuslay, Ronnel; Young, Wendy B.
CORPORATE SOURCE: Celera Genomics, South San Francisco, CA, 94080, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(17), 4567-4570
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 4-amino-5-azaindole as an amidino-benzimidazole replacement is described. A series of potent and selective analogs were discovered and showed desirable ex vivo efficacy as measured by PT.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:548795 CAPLUS Full-text
DOCUMENT NUMBER: 145:180192
TITLE: Efforts toward oral bioavailability in factor VIIa inhibitors
AUTHOR(S): Vijaykumar, Dange; Rai, Roopa; Shaghafi, Michael; Ton, Tony; Torkelson, Steve; Leahy, Ellen M.; Riggs, Jennifer R.; Hu, Huiyong; Sprengeler, Paul A.; Shrader, William D.; O'Bryan, Colin; Cabuslay, Ronnell; Sanford, Ellen; Gjerstadt, Erik; Liu, Liang; Sukbuntherng, Juthamas; Young, Wendy B.
CORPORATE SOURCE: Celera, South San Francisco, CA, 94979, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(14), 3829-3832
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:180192
AB Efforts toward developing orally bioavailable factor VIIa inhibitors starting from parenteral lead compd. 1 are described. SAR resulted in improved physicochem. properties, leading to enhanced oral absorption in rat.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:453896 CAPLUS Full-text
DOCUMENT NUMBER: 145:55376
TITLE: Novel 5-azaindole factor VIIa inhibitors
AUTHOR(S): Riggs, Jennifer R.; Hu, Huiyong; Kolesnikov, Aleksandr; Leahy, Ellen M.; Wesson, Kieron E.; Shrader, William D.; Vijaykumar, Dange; Wahl, Troy A.; Tong, Zhiwei; Sprengeler, Paul A.; Green, Michael J.; Yu, Christine; Katz, Brad A.; Sanford, Ellen; Nguyen, Margaret; Cabuslay, Ronnel; Young, Wendy B.
CORPORATE SOURCE: Celera Genomics, South San Francisco, CA, 94080, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(12), 3197-3200
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:55376
AB The discovery and development of 5-azaindole factor VIIa inhibitors will be described.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:315166 CAPLUS Full-text
DOCUMENT NUMBER: 145:27905
TITLE: Discovery of novel hydroxy pyrazole based factor IXa inhibitor
AUTHOR(S): Vijaykumar, Dange; Sprengeler, Paul A.; Shaghafi, Michael; Spencer, Jeffrey R.; Katz, Brad A.; Yu, Christine; Rai, Roopa; Young, Wendy B.; Schultz, Brian; Janc, James
CORPORATE SOURCE: Celera, South San Francisco, CA, 94080, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(10), 2796-2799
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:27905
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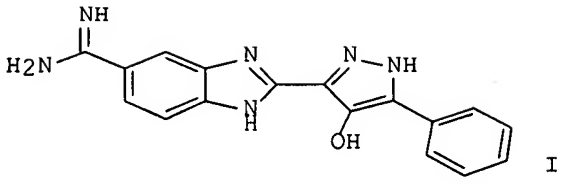

I

AB Synthesis and biol. data of a novel selective and efficacious factor IXa inhibitor I were described along with its crystal structure in factor VIIa.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:232886 CAPLUS Full-text
DOCUMENT NUMBER: 144:403785
TITLE: Discovery of novel heterocyclic factor VIIa inhibitors
AUTHOR(S): Rai, Roopa; Kolesnikov, Aleksandr; Sprengeler, Paul A.; Torkelson, Steven; Ton, Tony; Katz, Bradley A.; Yu, Christine; Hendrix, John; Shrader, William D.; Stephens, Robin; Cabuslay, Ronnell; Sanford, Ellen; Young, Wendy B.
CORPORATE SOURCE: Celera, South San Francisco, CA, 94080, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(8), 2270-2273
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:403785
AB Structure-activity relationships and binding mode of novel heterocyclic factor VIIa inhibitors will be described. In these inhibitors, a highly basic 5-amidinoindole moiety has been successfully replaced with a less basic 5-aminopyrrolo[3,2-b]pyridine scaffold.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:232880 CAPLUS Full-text
DOCUMENT NUMBER: 144:403784
TITLE: Factor VIIa inhibitors: Improved pharmacokinetic parameters
AUTHOR(S): Kolesnikov, Aleksandr; Rai, Roopa; Young, Wendy B.; Mordenti, Joyce; Liu, Liang; Torkelson, Steven; Shrader, William D.; Leahy, Ellen M.; Hu, Huiyong; Gjerstad, Erik; Janc, James; Katz, Bradley A.; Sprengeler, Paul A.
CORPORATE SOURCE: Celera Genomics, South San Francisco, CA, 94080, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(8), 2243-2246
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:403784

AB Efforts to improve the potency and pharmacokinetic properties of small mol. factor VIIa inhibitors are described. Small structural modifications to existing leads allow the modulation of half-life and clearance, potentially making these compds. suitable candidates for drug development.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:232876 CAPLUS Full-text
DOCUMENT NUMBER: 144:439762
TITLE: Factor VIIa inhibitors: A prodrug strategy to improve oral bioavailability
AUTHOR(S): Riggs, Jennifer R.; Kolesnikov, Aleksandr; Hendrix, John; Young, Wendy B.; Shrader, William D.; Vijaykumar, Dange; Stephens, Robin; Liu, Liang; Pan, Lin; Mordenti, Joyce; Green, Michael J.; Sukbuntherng, Juthamas
CORPORATE SOURCE: Celera Genomics, South San Francisco, CA, 94080, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(8), 2224-2228
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have developed a series of potent and selective factor VIIa inhibitors based on the 2-[5-(5-carbamimidoyl-1H-benzoimidazol-2-yl)-6-hydroxy- biphenyl-3-yl]-succinic acid scaffold. These amidine-contg. compds. have low oral bioavailability. Herein, we describe our efforts to improve the oral bioavailability of the parent amidine via a prodrug strategy where the amidine basicity and polarity were reduced with either an alkoxy-amidine or a carbamate prodrug.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:188923 CAPLUS Full-text
DOCUMENT NUMBER: 144:403775
TITLE: Factor VIIa inhibitors: Chemical optimization, preclinical pharmacokinetics, pharmacodynamics, and efficacy in an arterial baboon thrombosis model
AUTHOR(S): Young, Wendy B.; Mordenti, Joyce; Torkelson, Steven; Shrader, William D.; Kolesnikov, Aleksandr; Rai, Roopa; Liu, Liang; Hu, Huiyong; Leahy, Ellen M.; Green, Michael J.; Sprengeler, Paul A.; Katz, Bradley A.; Yu, Christine; Janc, James W.; Elrod, Kyle C.; Marzec, Ulla M.; Hanson, Stephen R.
CORPORATE SOURCE: Celera Genomics, South San Francisco, CA, 94080, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(7), 2037-2041
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:403775
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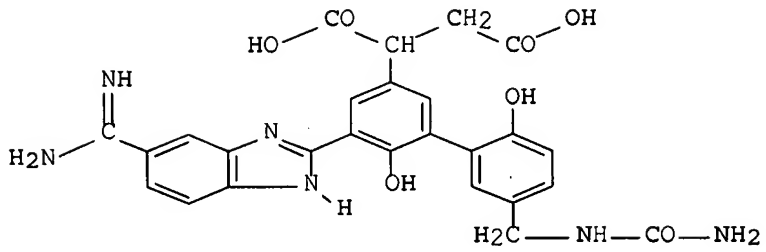

I

AB Highly selective and potent factor VIIa-tissue factor (fVIIa .cntdot. TF) complex inhibitors were generated through structure-based design. The pharmacokinetic properties of an optimized analog I were characterized in several preclin. species, demonstrating pharmacokinetic characteristics suitable for once-a-day dosing in humans. Analog I inhibited platelet and fibrin deposition in a dose-dependent manner after i.v. administration in a baboon thrombosis model, and a pharmacodynamic concn.-response model was developed to describe the platelet deposition data. Results for heparin and enoxaparin (Lovenox) in the baboon model are also presented.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:188922 CAPLUS Full-text

DOCUMENT NUMBER: 144:403774

TITLE: Small molecule inhibitors of plasma kallikrein

AUTHOR(S): Young, Wendy B.; Rai, Roopa; Shrader, William D.; Burgess-Henry, Jana; Hu, Huiyong; Elrod, Kyle C.; Sprengeler, Paul A.; Katz, Bradley A.; Sukbuntherng, Juthamas; Mordenti, Joyce

CORPORATE SOURCE: Celera Genomics, South San Francisco, CA, 94080, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(7), 2034-2036
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 144:403774

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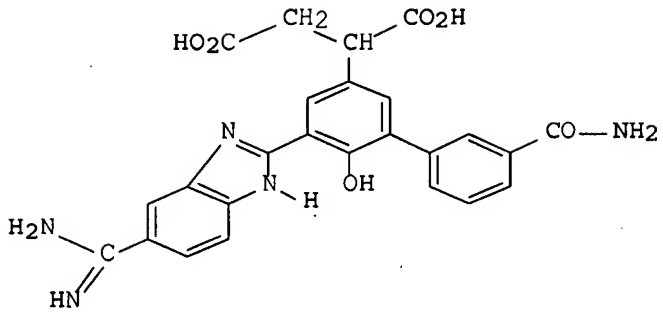

I

AB Plasma kallikrein is a serine protease that is involved in pathways of inflammation, complement fixation, coagulation, and fibrinolysis. Herein, we describe the SAR and structural binding modes of a series of inhibitors of plasma kallikrein as well as the pharmacokinetics of a lead analog I in rat.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:128504 CAPLUS Full-text

DOCUMENT NUMBER: 144:285642

TITLE: Factor VIIa inhibitors: Gaining selectivity within the trypsin family

AUTHOR(S): Shrader, William D.; Kolesnikov, Aleksandr; Burgess-Henry, Jana; Rai, Roopa; Hendrix, John; Hu, Huiyong; Torkelson, Steve; Ton, Tony; Young, Wendy B.; Katz, Bradley A.; Yu, Christine; Tang, Jie; Cabuslay, Ronnel; Sanford, Ellen; Janc, James W.; Sprengeler, Paul A.

CORPORATE SOURCE: Celera Genomics, South San Francisco, CA, 94080, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(6), 1596-1600
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 144:285642

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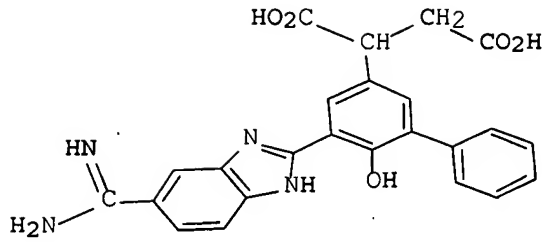

I

AB Within the trypsin family of coagulation proteases, obtaining highly selective inhibitors of factor VIIa has been challenging. We report a series of factor VIIa (fVIIa) inhibitors based on the 5-amidino-2-(2- hydroxy-biphenyl-3-yl)-benzimidazole (I) scaffold with potency for fVIIa and high selectivity against factors IIa, Xa, and trypsin. With this scaffold class, we propose that a unique hydrogen bond interaction between a hydroxyl on the distal ring of the biaryl system and the backbone carbonyl of fVIIa lysine-192 provides a basis for enhanced selectivity and potency for fVIIa.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1330357 CAPLUS Full-text
DOCUMENT NUMBER: 144:69827
TITLE: Dihydroxybiphenylacetamides as Factor VIIa inhibitors, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Torkelson, Steven M.; Vojkovsky, Tomas
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005121102	A2	20051222	WO 2005-US19420	20050602
WO 2005121102	A3	20060126		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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CA 2569170	A1	20051222	CA 2005-2569170	20050602

EP 1751114	A2	20070214	EP 2005-790220		20050602
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IN 2006KN03600	A	20070615	IN 2006-KN3600		20061201
PRIORITY APPLN. INFO.:			US 2004-576330P	P	20040602
			WO 2005-US19420	W	20050602

OTHER SOURCE(S): CASREACT 144:69827
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a group of 12 different dihydroxybiphenylacetamides, e.g., I, which are inhibitors of Factors VIIa, IXa, Xa, and XIa, in particular Factor VIIa. The invention also relates to the prepn. of these dihydroxybiphenylacetamides, pharmaceutical compns. comprising a therapeutically effective amt. of a compd. of the invention and a pharmaceutically acceptable carrier, optionally in combination with another anticoagulant agent, as well as to the use of the compns. in the treatment of a thromboembolic disorder. C-Dimethylation of 4-methoxyphenylacetonitrile followed by acid hydrolysis, O-demethylation, esterification, formylation, and bromination gave methylpropanoate II. 3-Bromo-4-methoxybenzonitrile was converted to the corresponding boronic acid, coupled with O-methylated II, and cyclized with 3,4- diaminobenzamidine (prepn. in 3 steps from 4-amino-3-nitrobenzonitrile is given) to give dimethoxybiphenylacetate III. Compd. III underwent demethylation to the dihydroxybiphenylacetic acid followed by amidation, hydrogenation of the nitrile, acylation with (S)-2,2-dimethyl-1,3-dioxolane-4-carboxylate, and ring cleavage, resulting in the formation of I. The compds. of the invention express inhibition of Factor VIIa and Factor Xa (no data).

L8 ANSWER 12 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1314797 CAPLUS Full-text
DOCUMENT NUMBER: 144:51583
TITLE: Preparation of benzimidazole-5-carboxamidine derivatives as factor VIIa inhibitors
INVENTOR(S): Dickman, Daniel A.; Kumar, Dange Vijay; O'Bryan, Colin; Rai, Roopa; Shrader, William Dvorak
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005118554	A2	20051215	WO 2005-US19394	20050602
WO 2005118554	A3	20060518		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,				

SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2005250470	A1	20051215	AU 2005-250470	20050602
CA 2569163	A1	20051215	CA 2005-2569163	20050602
EP 1761504	A2	20070314	EP 2005-757137	20050602
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1964951	A	20070516	CN 2005-80017896	20050602
IN 2006KN03598	A	20070615	IN 2006-KN3598	20061201
PRIORITY APPLN. INFO.:			US 2004-576382P	P 20040602
			WO 2005-US19394	W 20050602

OTHER SOURCE(S): CASREACT 144:51583; MARPAT 144:51583

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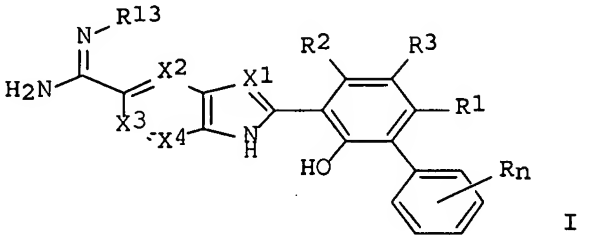
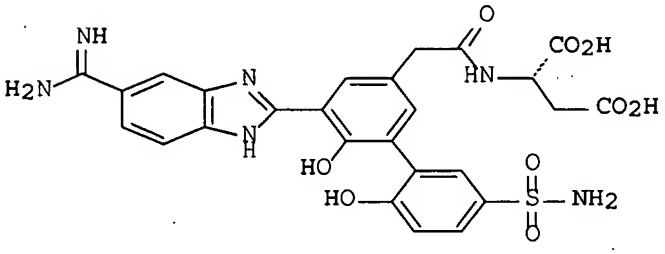


I



II

AB Title compds. represented by the formula I [wherein X1-X4 = independently N or CR4; R4 = H, alkyl or halo; with the proviso that not more than three of X1-X4 are -N-; R1 = H, alkyl, halo, carboxy or aminocarbonyl; R2 = H, alkyl or halo; R3 = dicarboxyalkylaminocarbonylalkyl or dicarboxyalkylaminocarbonylcycloalkyl; R = independently H, alkyl, halo, hydroxy, etc.; n = 3; R13 = H, hydroxy, alkoxy, etc.; and a zwitterion or a pharmaceutically acceptable salt thereof] were prepd. as factor VIIa inhibitors. For example, II was provided in a multi-step synthesis starting from Me 2-(4-hydroxyphenyl)acetate. I showed inhibition of Factor VIIa and Xa, and their pharmaceutical compns. were also described.

L8 ANSWER 13 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:395282 CAPLUS Full-text
DOCUMENT NUMBER: 142:447214

TITLE: Preparation of triarylcarboxamidines as antiprotozoals.

INVENTOR(S): Boykin, David W.; Tidwell, Richard R.; Wilson, W. David; Brun, Reto; Mohamed, A. Ismail

PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA; Georgia State University Research Foundation, Inc.

SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

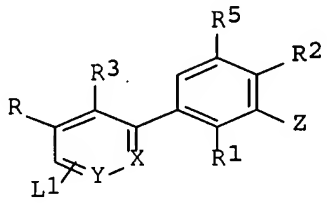
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005040132	A1	20050506	WO 2004-US35311	20041025
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004284091	A1	20050506	AU 2004-284091	20041025
CA 2543079	A1	20050506	CA 2004-2543079	20041025
US 2005148646	A1	20050707	US 2004-972715	20041025
EP 1682518	A1	20060726	EP 2004-796320	20041025
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1898214	A	20070117	CN 2004-80038745	20041025
JP 2007509176	T	20070412	JP 2006-536889	20041025

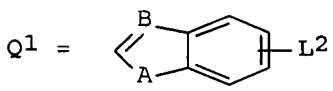
PRIORITY APPLN. INFO.: US 2003-514168P P 20031024
WO 2004-US35311 W 20041025

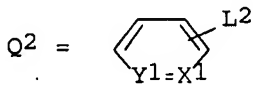
OTHER SOURCE(S): CASREACT 142:447214; MARPAT 142:447214

GI



I





AB Title compds. [I; X = CH, N, O, S; Y = X, null; R1 = H, alkyl, halo, alkoxy, aryloxy, aralkoxy; R2-R5 = H, alkyl, halo, OH, alkoxy, aryloxy, aralkoxy; Z = Q1, Q2; A = O, S, NR6; R6 = H, alkyl; B = O, S, N; X1 = CH, N, O, S; Y1 = X1,

null; L1, L2 = C(:NR7)NR8R9, NHC(:NR7)NR8R9, CH:NNR10C(:NR7)NR8R9, etc.; R7 = H, alkyl, OH, alkoxyalkyl, cycloalkyl, aryl, aralkyl, alkoxy, hydroxyalkyl, acyloxy, aminoalkyl, etc.; R8-R10 = H, alkyl, OH, alkoxyalkyl, cycloalkyl, aryl, aralkyl, alkoxy, acyloxy, aminoalkyl, etc.; R7R8 = alkyl, hydroxyalkyl, alkylene, etc.], were prepd. Thus, 2-[3-(5-carbamimidoylpyridin-2-yl)phenyl]-1H-benzimidazole-5- carboxamidine acetate salt (prepn. from 2-chloro-5-cyanopyridine, 3-formylphenylboronic acid, and 3,4-diaminobenzonitrile given) showed an IC50 = 15 nM against Trypanosoma brucei rhodesiense (Tbr) and gave a complete cure of STIP900 Tbr in mice. Novel dicationic, heterocyclic triaryl compds. are useful in the treatment of microbial infections, such as Trypanosoma brucei rhodesiense infection and Plasmodium falciparum infection. These compds. are accordingly useful in treating second-stage human African trypanosomiasis. Pharmaceutical formulations comprising these compds. can be used in methods of treating microbial infections.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:324127 CAPLUS Full-text

DOCUMENT NUMBER: 142:373841

TITLE: Preparation of novel amidines for treating microbial infections like human African trypanosomiasis and falciparum malaria

INVENTOR(S): Tidwell, Richard R.; Boykin, David; Brun, Reto; Stephens, Chad E.; Kumar, Arvind

PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA; Georgia State University Research Foundation, Inc.

SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005033065	A1	20050414	WO 2003-US27963	20030905
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2537791	A1	20050414	CA 2003-2537791	20030905
AU 2003265967	A1	20050421	AU 2003-265967	20030905
EP 1663959	A1	20060607	EP 2003-818831	20030905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2007521237	T	20070802	JP 2005-509376	20030905
US 2007088067	A1	20070419	US 2006-570584	20061117

PRIORITY APPLN. INFO.: WO 2003-US27963 W 20030905

OTHER SOURCE(S): CASREACT 142:373841; MARPAT 142:373841

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Novel amidine and diamidine compds. (1st of 7 claimed Markush formulas shown as I; variables defined below; e.g. 4,4'-bis(6-amidinobenzimidazol-2- yl)-1,2-diphenylethane tetrahydrochloride (II)) may be useful in the treatment of microbial infections, including mycobacterial, fungal and protozoal infections. Pharmaceutical formulations comprising these compds. can be used in methods of treating microbial infections. Neither pharmacol. activity nor therapeutic use is claimed, but the effectiveness of 11 examples of the claimed compds. against Trypanosoma rhodesiense and Plasmodium falciparum is tabulated. Although the methods of prepn. are not claimed, 9 example prepns. of claimed compds. and intermediates are included. For example, II was prepd. (64 %) from 4,4'-diformyl-1,2- diphenylethane, 4-amidino-1,2-phenylenediamine hydrochloride hemihydrate and 1,4-benzoquinone in EtOH. For I: X' and X'' = alkyl, alkylene, O, oxy, oxyalkyl, alkyloxy, alkyloxyalkyl, and -C(O)NH(CH2)q-; m, n, p, and q = 0-10; L = hydroxyalkyl, 1,2-oxazole, 1,3-oxazole, Ph, naphthyl, pyrimidine, alkyl-substituted pyrimidine and -CH(CO2R11)- (R11 = H or alkyl); R1-R10 = H, alkyl, hydroxy, oxyalkyl, alkyloxy, halo, aryl, and Y, wherein at least one of R1-R10 = Y, and Y = -C(:NR12)NR13R14, -CH:NNHC(:NR12)NR13R14, and -NHC(NR12)NR13R14 (R12 = H, hydroxy, cycloalkyl, aryl, aralkyl, alkoxyl, hydroxycycloalkyl, alkoxycycloalkyl, hydroxyalkyl, aminoalkyl, acyloxy, and alkylaminoalkyl; R13 and R14 = H, hydroxy, alkyl, alkoxyalkyl, cycloalkyl, aryl, aralkyl, hydroxyalkyl, aminoalkyl, and alkylaminoalkyl; or R12 and R13 together = C2-C10 alkyl, hydroxyalkyl, or alkylene; or R12 and R13 together = (R15)j-substituted o-phenylene (j = 1-3, and R15 is H or Y)).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:244323 CAPLUS Full-text

DOCUMENT NUMBER: 142:475246

TITLE: 3D-QSAR CoMFA studies on trypsin-like serine protease inhibitors: a comparative selectivity analysis

AUTHOR(S): Bhongade, Bhoomendra A.; Gouripur, Veerappa V.; Gadad, Andanappa K.

CORPORATE SOURCE: Department of Medicinal Chemistry, College of Pharmacy, J. N. Medical College, Belgaum, 590 010, India

SOURCE: Bioorganic & Medicinal Chemistry (2005), 13(8), 2773-2782
CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of indole/benzoimidazole-5-carboxamidines have been reported to inhibit various trypsin-like serine proteases viz. uPA, tPA, factor Xa, thrombin, plasmin, and trypsin, which are involved in various types of pathophysiol. conditions such as cancer progression, thrombosis etc. Inhibition of these protease enzymes may serve as therapeutic agents in various types of cancer as well serve as anticoagulant or antithrombotic agents. The dual inhibitory action may result in poor clin. candidates. 3D-QSAR models were generated for indole/benzoimidazole-5-carboxamidines using the CoMFA technique to study their selectivity trends toward various trypsin-like serine proteases. Mol. superimposition was carried out on the template structure using atom-based RMS fit method. The CoMFA models were established from the training set of 25-29 mols. and validated by predicting the activities of seven-eight test set mols. The CoMFA models generated using steric and electrostatic fields for tPA, fXa, thrombin, plasmin, and trypsin

inhibition exhibited better statistical significance than the CoMFA models generated using ClogP as an addnl. descriptor. Thus, the validated CoMFA models with steric and electrostatic fields were used to generate 3D contour maps, which may provide possible modification of mols. for better selectivity/activity. The present 3D-QSAR studies emphasize the selectivity trends of indole/benzoimidazole-5- carboxamidines, which may be obliging in designing novel selective serine protease inhibitors of therapeutic interest.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:917422 CAPLUS Full-text

DOCUMENT NUMBER: 142:88665

TITLE: Dissecting and Designing Inhibitor Selectivity Determinants at the S1 Site Using an Artificial Ala190 Protease (Ala190 uPA)

AUTHOR(S): Katz, Bradley A.; Luong, Christine; Ho, Joseph D.; Somoza, John R.; Gjerstad, Erik; Tang, Jie; Williams, Steven R.; Verner, Erik; Mackman, Richard L.; Young, Wendy B.; Sprengeler, Paul A.; Chan, Hedy; Mortara, Kyle; Janc, James W.; McGrath, Mary E.

CORPORATE SOURCE: Celera, South San Francisco, CA, 94080, USA

SOURCE: Journal of Molecular Biology (2004), 344(2), 527-547
CODEN: JMOBAK; ISSN: 0022-2836

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A site-directed mutant of the serine protease urokinase-type plasminogen activator (uPA), was produced to assess the contribution of the Ser190 side-chain to the affinity and selectivity of lead uPA inhibitors in the absence of other differences present in comparisons of natural proteases. Crystallog. and enzymol. involving WT and Ala190 uPA were used to calc. free energy binding contributions of hydrogen bonds involving the Ser190 hydroxyl group (O.gamma.Ser190) responsible for the remarkable selectivity of 6-halo-5-amidinoindole and 6-halo-5-amidinobenzimidazole inhibitors toward uPA and against natural Ala190 protease anti-targets. Crystal structures of uPA complexes of novel, active site-directed arylguanidine and 2-aminobenzimidazole inhibitors of WT uPA, together with assocd. Ki values for WT and Ala190 uPA, also indicate a significant role of Ser190 in the binding of these classes of uPA inhibitors. Structures and assocd. Ki values for a lead inhibitor (CA-11) bound to uPA and to five other proteases, as well as for other leads bound to multiple proteases, help reveal the features responsible for the potency (Ki=11 nM) and selectivity of the remarkably small inhibitor, CA-11. The 6-fluoro-5- amidinobenzimidzole, CA-11, is more than 1000-fold selective against natural Ala190 protease anti-targets, and more than 100-fold selective against other Ser190 anti-targets.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:791709 CAPLUS Full-text

DOCUMENT NUMBER: 141:325174

TITLE: Dicationic biphenyl benzimidazole derivatives as antiprotozoal agents

AUTHOR(S): Ismail, Mohamed A.; Brun, Reto; Wenzler, Tanja; Tanious, Farial A.; Wilson, W. David; Boykin, David W.

CORPORATE SOURCE: Department of Chemistry and Center for Biotechnology and Drug Design, Georgia State University, Atlanta, GA, 30303-3083, USA

SOURCE: Bioorganic & Medicinal Chemistry (2004), 12(20),

5405-5413
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:325174

AB A series of biphenyl benzimidazoles diamidines were synthesized from their resp. diamidoximes, through the bis-O-acetoxyamidoxime followed by hydrogenation in glacial acetic acid/ethanol in the presence of Pd-C. The target compds. contain hydroxy and/or methoxy substituted 1,3-Ph groups as the central spacer between the two amidino bearing aryl groups. All of the diamidines showed strong DNA affinities as judged by high .DELTA.Tm values with poly(dA.cntdot.dT)2, which varied with structure and is discussed. Seven of the nine new diamidines gave in vitro IC50 values of approx. 30 nM or less vs. Trypanosoma brucei rhodesiense (T.b.r.). Generally the diamidines were less active vs. Plasmodium falciparum (P.f.), however one compd. exhibited excellent activity with an IC50 value of 2.1 nM. Five of the nine diamidines exhibited excellent in vivo activity in the trypanosomal STIB900 mouse model giving 3/4 or 4/4 cures at dosage of 20 mg/kg i.p. and three showed similar efficacy at dosage of 10 mg/kg or lower.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:610079 CAPLUS Full-text
DOCUMENT NUMBER: 141:157116
TITLE: Preparation of carbamimidoylheteroarylhydroxybiphenylcarboxylates as as Factor VIIa inhibitors
INVENTOR(S): Kolesnikov, Aleksandr; Torkelson, Steven M.; Vojkovsky, Tomas
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004062661	A1	20040729	WO 2003-US41636		20031223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003300106	A1	20040810	AU 2003-300106		20031223
PRIORITY APPLN. INFO.:			US 2003-439083P	P	20030108
			WO 2003-US41636	W	20031223

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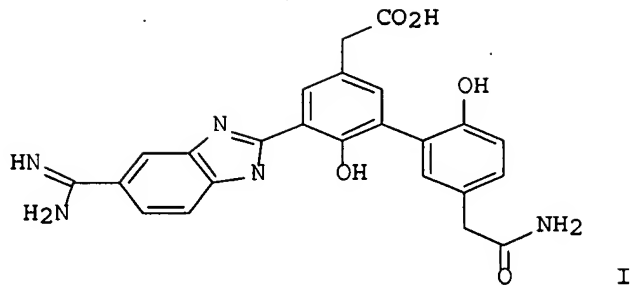

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AB 35 Title compds. are claimed, as is use of the compds. for treatment of thromboembolic disorders and cancer (no data). Thus, Me 2-[5-formyl-6,2'-bis(2-methoxyethoxymethoxy)-5'-[[(2-methoxyethoxymethyl)carbamoyl]methyl]biphenyl-3-yl]acetate (prepn. given) was refluxed 7 h with 3,4-diaminobenzamidine hydrochloride and 1,4-benzoquinone in MeOH to give a crude product which was stirred 2 h with HCl in MeOH followed by treatment of the residue with aq. NaOH in MeOH to give title compd. (I).

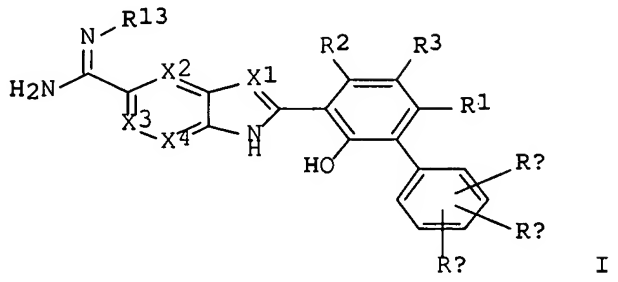
L8 ANSWER 19 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:493686 CAPLUS Full-text
DOCUMENT NUMBER: 141:54342
TITLE: Preparation of 2-(2-hydroxybiphenyl-3-yl)-1H-benzimidazole-5-carboxamidine derivatives as factor VIIa inhibitors
INVENTOR(S): Kolesnikov, Aleksandr; Rai, Roopa; Shrader, William Dvorak; Torkelson, Steven M.; Wesson, Kieron E.; Young, Wendy B.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050637	A2	20040617	WO 2003-US38635	20031203
WO 2004050637	A3	20040902		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2507707	A1	20040617	CA 2003-2507707	20031203
AU 2003302238	A1	20040623	AU 2003-302238	20031203
EP 1569912	A2	20050907	EP 2003-810056	20031203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

CN 1745070	A	20060308	CN 2003-80109503		20031203
JP 2006515839	T	20060608	JP 2004-557602		20031203
IN 2005KN01065	A	20060818	IN 2005-KN1065		20050603
US 2006205942	A1	20060914	US 2006-537115		20060320
PRIORITY APPLN. INFO.:			US 2002-430981P	P	20021203
			WO 2003-US38635	W	20031203

OTHER SOURCE(S): MARPAT 141:54342

GI



I

AB The title compds. (I) [X1-X4 = independently N or CR5 (wherein R5 = H, alkyl, or halo) with the proviso that not more than three of X1-X4 are N; R1 = H, alkyl, halo, CO2H, CONH2; R2 = H, alkyl, halo; R3 = H, halo, alkyl, alkoxy, haloalkyl, haloalkoxy, haloalkylthio, haloalkylsulfonyl, cyanoalkyl, tetrazol-5-yl, tetrazol-5-ylalkyl, hydroxyalkylcarbonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, oxalyl, NHSO2R (where R = alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl or heterocycloalkylalkyl), SO2NHCOR6 (where R6 = alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, or heterocycloalkylalkyl), SO3H, sulfonylalkyl, each N-(un)substituted CONH2, CH(CF3)NH2, or COCONH2; Rx = H, alkyl, alkylthio, halo, HO, hydroxyalkyl, alkoxy, SO2NH2, alkylaminosulfonyl, dialkylaminosulfonyl, NO2; Ry = H, alkyl, halo; Rz = H, alkyl, haloalkyl, cycloalkyl, alkylthio, halo, HO, hydroxyalkyl, nitro, cyano, alkoxy, alkoxyalkyl, alkoxyalkyloxy, hydroxyalkyloxy, aminoalkyloxy, carboxyalkyloxy, aminocarbonylalkyloxy, haloalkoxy, CO2H, etc.; R13 = H, HO, C1-10 alkoxy, COR35 (where R35 = alkyl, aryl, haloalkyl, or cyanoalkyl), CO2R36 (where R36 = alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, acyl, aryl, or haloalkyl)] and individual isomers, mixt. of isomers, or pharmaceutically acceptable salts thereof are prepd. These compds. are novel inhibitors of factors VIIa, IXa, Xa, XIa, in particular factor VIIa (no data). Pharmaceutical compns. comprising these inhibitors are useful for treating a disease in an animal mediated by factor VIIa, thromboembolic disorders, cancer or rheumatoid arthritis, in particular thromboembolic disorders. Thus, 1-tert-butyl-3-[[3'-formyl- 6,2'-bis(2-methoxyethoxymethoxy)biphenyl-3-yl]methyl]urea, 3,4-diaminobenzamidine hydrochloride, and 1,4-benzoquinone were combined in methanol, heated at 60.degree., and stirred for 2 h to give 2-[5'-(3-tert-butylureidomethyl)-2,2'-bis(2-methoxyethoxymethoxy)biphenyl- 3-yl]-1H-benzimidazole-5-carboximidamide which was dissolved in 4 M hydrogen chloride in dioxane and the soln. and stirred at room temp. for 1 h to give 2-(2,2'-dihydroxy-5'-ureidomethylbiphenyl-3-yl)-1H-benzimidazole- 5-carboximidamide hydrochloride.

L8 ANSWER 20 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:339493 CAPLUS Full-text

DOCUMENT NUMBER: 141:116428
TITLE: 3D-QSAR CoMFA/CoMSIA studies on urokinase plasminogen activator (uPA) inhibitors: a strategic design in novel anticancer agents
AUTHOR(S): Bhongade, B. A.; Gadad, A. K.
CORPORATE SOURCE: College of Pharmacy, Department of Medicinal Chemistry, J. N. Medical College, Belgaum, 590010, India
SOURCE: Bioorganic & Medicinal Chemistry (2004), 12(10), 2797-2805
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Comparative mol. field anal. (CoMFA) and comparative mol. similarity indexes anal. (CoMSIA) was performed on a series of indole/benzoimidazole- 5-carboxamidines as urokinase plasminogen activator (uPA) inhibitors. The ligand mol. superimposition on template structure was performed by atom/shape-based RMS fit, multifit, and RMSD fit methods. The removal of two outliers from the initial training set of 30 mols. improved the predictivity of the models. The statistically significant model was established from 28 mols., which were validated by evaluation of test set of nine compds. The atom-based RMS alignment yielded best predictive CoMFA model (r2cv=0.611, r2cnv=0.778, F value=43.825, r2bs=0.842, r2pred=0.616 with two components) while the CoMSIA model yielded (r2cv=0.499, r2cnv=0.976, F value=96.36, r2bs=0.993, r2pred=0.694 with eight components). The contour maps obtained from 3D-QSAR studies were appraised for the activity trends of the mols. analyzed. The results indicate that the steric, electrostatic, and hydrogen bond donor/acceptor substituents play significant role in uPA activity and selectivity of these compds. The data generated from the present study can be used as putative pharmacophore in the design of novel, potent, and selective urokinase plasminogen activator inhibitors as cancer therapeutics.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:991295 CAPLUS Full-text
DOCUMENT NUMBER: 140:35966
TITLE: Amidine derivatives for treating amyloidosis and neurodegenerative diseases
INVENTOR(S): Chalifour, Robert J.; Kong, Xianqi; Wu, Xinfu; Lu, Wenshuo; Tidwell, Richard R.; Boykin, David
PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA; Georgia State University Research Foundation, Inc.
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003103598	A2	20031218	WO 2003-US17992	20030609
WO 2003103598	A3	20060309		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,

TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2488493	A1	20031218	CA 2003-2488493	20030609
AU 2003251418	A1	20031222	AU 2003-251418	20030609
EP 1572129	A2	20050914	EP 2003-757414	20030609
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006501160	T	20060112	JP 2004-510719	20030609
US 2004147531	A1	20040729	US 2003-731463	20031205
US 2007021483	A1	20070125	US 2006-335171	20060119
PRIORITY APPLN. INFO.:			US 2002-387001P	P 20020607
			US 2001-316761P	P 20010831
			US 2002-234643	A1 20020903
			WO 2003-US17992	W 20030609
			US 2003-731463	B1 20031205

AB The present invention relates to the use of amidine compds. in the treatment of amyloid related diseases. In particular, the invention relates to a method of treating or preventing an amyloid-related disease in a subject comprising administering to the subject a therapeutic amt. of an amidine compd. Among the compds. for use according to the invention are those according to the following Formulas, such that, when administered, amyloid fibril formation, neurodegeneration, or cellular toxicity is reduced or inhibited.

Not OOP

L8 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:656754 CAPLUS Full-text
DOCUMENT NUMBER: 139:197482
TITLE: Preparation of 2-[5-(5-carbamimidoyl-1H-heteroaryl)]-6-hydroxybiphenyl derivatives as factor VIIa inhibitors
INVENTOR(S): Kolesnikov, Aleksandr; Rai, Roopa; Shrader, William Dvorak; Young, Wendy B.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068756	A1	20030821	WO 2003-US4081	20030212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2474195	A1	20030821	CA 2003-2474195	20030212
AU 2003215158	A1	20030904	AU 2003-215158	20030212
EP 1474400	A1	20041110	EP 2003-710972	20030212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

JP 2005523279	T	20050804	JP 2003-567887		20030212
US 2005203094	A1	20050915	US 2005-504119		20050505
PRIORITY APPLN. INFO.:			US 2002-356473P	P	20020213
			US 2003-439043P	P	20030108
			WO 2003-US4081	W	20030212

OTHER SOURCE(S): MARPAT 139:197482
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X1-X4 = N, (un)substituted CH; R1, R2 = H, alkyl, hydroxyalkyl, halogen; R3 = (un)substituted hydroxyalkyl, carboxyalkyl, carboxycycloalkyl, carboxyalkoxy, dicarboxyalkoxy, lactam; R4 = (un)substituted Ph; Y = H, OH, (un)substituted alkoxy, CO2H] were prepd. as inhibitors of factor VIIa and Xa (no data). Thus, the benzimidazole II was prepd. from 4-HOC6H4CH:C(CO2Me)2 and 3,4-(H2N)2C6H3C(:NH)NH2.HCl in 9 steps.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 23 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:343069 CAPLUS Full-text
DOCUMENT NUMBER: 139:226287
TITLE: Elaborate Manifold of Short Hydrogen Bond Arrays Mediating Binding of Active Site-directed Serine Protease Inhibitors
AUTHOR(S): Katz, Bradley A.; Elrod, Kyle; Verner, Erik; Mackman, Richard L.; Luong, Christine; Shrader, William D.; Sendzik, Martin; Spencer, Jeffrey R.; Sprengeler, Paul A.; Kolesnikov, Aleks; Tai, Vincent W.-F.; Hui, Hon C.; Guy Breitenbucher, J.; Allen, Darin; Janc, James W.
CORPORATE SOURCE: Celera, South San Francisco, CA, 94080, USA
SOURCE: Journal of Molecular Biology (2003), 329(1), 93-120
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An extensive structural manifold of short hydrogen bond-mediated, active site-directed, serine protease inhibition motifs is revealed in a set of over 300 crystal structures involving a large suite of small mol. inhibitors (2-(2-phenol)-indoles and 2-(2-phenol)-benzimidazoles) detd. over a wide range of pH (3.5-11.4). The active site hydrogen-bonding mode was found to vary markedly with pH, with the steric and electronic properties of the inhibitor, and with the type of protease (trypsin, thrombin or urokinase type plasminogen activator (uPA)). The pH dependence of the active site hydrogen-bonding motif is often intricate, constituting a distinct fingerprint of each complex. Isosteric replacements or minor substitutions within the inhibitor that modulate the pKa of the phenol hydroxyl involved in short hydrogen bonding, or that affect steric interactions distal to the active site, can significantly shift the pH-dependent structural profile characteristic of the parent scaffold, or produce active site-binding motifs unique to the bound analog. Ionization equil. at the active site assocd. with inhibitor binding are probed in a series of the protease-inhibitor complexes through anal. of the pH dependence of the structure and environment of the active site-binding groups involved in short hydrogen bond arrays. Structures detd. at high pH (>11), suggest that the pKa of His57 is dramatically elevated, to a value as high as .apprx.11 in certain complexes. Ki values involving uPA and trypsin detd. as

a function of pH for a set of inhibitors show pronounced parabolic pH dependence, the pH for optimal inhibition governed by the pKa of the inhibitor phenol involved in short hydrogen bonds. Comparison of structures of trypsin, thrombin and uPA, each bound by the same inhibitor, highlights important structural variations in the S1 and active sites accessible for engineering notable selectivity into remarkably small mols. with low nanomolar Ki values.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:173414 CAPLUS Full-text

DOCUMENT NUMBER: 138:215350

TITLE: Amidine derivatives for treating amyloid-related diseases

INVENTOR(S): Chalifour, Robert J.; Kong, Xianqi; Wu, Xinfu; Lu, Wenshuo

PATENT ASSIGNEE(S): Neurochem Inc., Can.

SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003017994	A1	20030306	WO 2002-CA1353	20020903
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2455497	A1	20030306	CA 2002-2455497	20020903
AU 2002325117	A1	20030310	AU 2002-325117	20020903
US 2004006092	A1	20040108	US 2002-234643	20020903
EP 1420773	A1	20040526	EP 2002-758012	20020903
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002012078	A	20040928	BR 2002-12078	20020903
JP 2005504053	T	20050210	JP 2003-522514	20020903
CN 1658852	A	20050824	CN 2002-815770	20020903
US 2004147531	A1	20040729	US 2003-731463	20031205
IN 2004CN00219	A	20051209	IN 2004-CN219	20040203
NO 2004000497	A	20040414	NO 2004-497	20040204
MX 2004PA01153	A	20050217	MX 2004-PA1153	20040206
US 2007021483	A1	20070125	US 2006-335171	20060119
PRIORITY APPLN. INFO.:			US 2001-316761P	P 20010831
			US 2002-387001P	P 20020607
			US 2002-234643	A1 20020903
			WO 2002-CA1353	W 20020903
			US 2003-731463	B1 20031205

OTHER SOURCE(S): MARPAT 138:215350

AB The invention discloses the use of amidine compds. in the treatment of amyloid-related diseases (e.g. Alzheimer's disease, Down's syndrome, type II diabetes). In particular, the invention discloses a method for treating or

preventing an amyloid-related disease in a subject comprising administering to the subject a therapeutic amt. of an amidine compd. The compds. of the invention (Markush included) are such that, when administered, reduce or inhibit amyloid fibril formation, neurodegeneration, or cellular toxicity. Compd. prepn. is described.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:58259 CAPLUS Full-text
DOCUMENT NUMBER: 138:117652
TITLE: 2-[5-(5-carbamimidoyl-1H-heteroaryl)-6-hydroxybiphenyl-3-yl]succinic acid derivatives as factor VIIa inhibitors
INVENTOR(S): Hu, Huiyong; Kolesnikov, Aleksandr; Sperandio, David; Young, Wendy Beth; Shrader, William Dvorak
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003006670	A2	20030123	WO 2002-US21340		20020703
WO 2003006670	A3	20030522			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002313655	A1	20030129	AU 2002-313655		20020703
US 2003114457	A1	20030619	US 2002-190147		20020703
US 2005176797	A1	20050811	US 2004-940001		20040913
PRIORITY APPLN. INFO.:			US 2001-303953P	P	20010709
			US 2002-351054P	P	20020122
			US 2002-190147	A1	20020703
			WO 2002-US21340	W	20020703

Not opd

OTHER SOURCE(S): MARPAT 138:117652

AB The present invention relates to derivs. of 2-[5-(5-carbamimidoyl-1H-heteroaryl)-6-hydroxybiphenyl-3-yl]succinic acid as inhibitors of Factors VIIa, IXa, Xa, XIa, in particular Factor VIIa, pharmaceutical compns. comprising these inhibitors, and methods for using these inhibitors for treating or preventing thromboembolic disorders. For example, 2-[5-(5-carbamimidoyl-1H-benzoimidazol-2-yl)-6-hydroxy-3'-nitro-biphenyl-3- yl]-succinic acid was prepd. by reaction of 2-(5-formyl-6-hydroxy-3'-nitro-biphenyl-3-yl)-succinic acid (0.3 g) and 3,4-diaminobenzamidine monohydrochloride (0.17 g) in a yield of 63%.

L8 ANSWER 26 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:57897 CAPLUS Full-text
DOCUMENT NUMBER: 138:122645

TITLE: Preparation of 2-[5-(5-Carbamimidoyl-1H-heteroaryl)-6-hydroxybiphenyl-3-yl]-succinic acid derivatives as factor VIIa inhibitors

INVENTOR(S): Hu, Huiyong; Kolesnikov, Aleksandr; Rai, Roopa; Shrader, William Dvorak; Young, Wendy Beth; Sperandio, David; Hendrix, John; Torkelson, Steve

PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003006011	A1	20030123	WO 2002-US21334	20020703
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2452391	A1	20030123	CA 2002-2452391	20020703
AU 2002316573	A1	20030129	AU 2002-316573	20020703
US 2003114457	A1	20030619	US 2002-190147	20020703
EP 1408963	A1	20040421	EP 2002-746886	20020703
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2005176797	A1	20050811	US 2004-940001	20040913

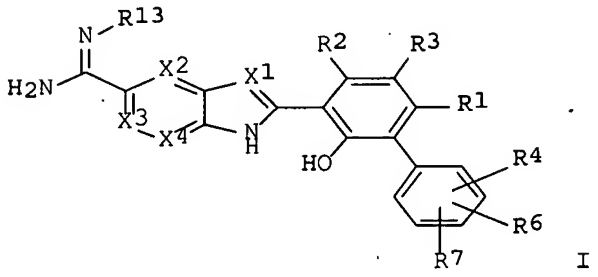
Not ODP

PRIORITY APPLN. INFO.:

US 2001-303953P	P	20010709
US 2002-351054P	P	20020122
US 2002-190147	A1	20020703
WO 2002-US21334	W	20020703

OTHER SOURCE(S): MARPAT 138:122645

GI



I

AB The present invention relates to [I; X1-X4 = N, CR5 (wherein R5 = H, alkyl); provided that not more than three of X1-X4 are N; R1, R2 = H, alkyl, halo; R3 = CO2R9, -(alkylene)-CO2R9, CR8(CO2R11)alkylene-CO2R9, -C(R8)[(alkylene)nCO2R9]CH(R10)CO2R11 (wherein R8 = H, alkyl, HO; R10 = H, alkyl; R8 and R10 together forms a covalent bond; R9, R11 = H, alkyl, haloalkyl, aryl, aralkyl); R4 = H, alkyl, alkylthio, halo, HO, hydroxyalkyl, alkoxy, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, NO2; R6 = H, alkyl, halo; R7 = H, alkyl, cycloalkyl, alkylthio, halo, HO, NO2, cyano, alkoxy, haloalkoxy, CO2H, alkoxycarbonyl, acylamino, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, etc.; R13 = H, HO, C1-10 alkoxy, COR35 (wherein R35 = alkyl, aryl, haloalkyl, cyanoalkyl, alkoxycarbonyl, hydroxyalkoxycarbonyl, acyloxycarbonyl, haloalkoxycarbonyl)] and individual isomers, mixts. of isomers, or pharmaceutically acceptable salts thereof which are novel inhibitors of factors VIIa, IXa, Xa, XIa, in particular factor VIIa (no data). Also disclosed are pharmaceutical compns. contg. the compds. I for treating or preventing a disease mediated by factor VIIa, in particular thromboembolic disorders. Also claimed is a method for inhibiting coagulation of a biol. sample. Thus, A mixt. of 0.3 g 2-(5-formyl-6-hydroxy-3'-nitrobiphenyl-3- yl)succinic acid, 0.17 g, 3,4-diaminobenzamidine monohydrochloride, and 0.097 g benzoquinone in 50 mL ethanol was heated for approx. 4 h to give, after purifn. by reverse phase HPLC (gradient, acetonitrile/0.02 N aq. HCl) to give 63% 2-[5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-6-hydroxy-3'- nitrobiphenyl-3-yl]succinic acid.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:680206 CAPLUS Full-text

DOCUMENT NUMBER: 137:365440

TITLE: Contribution of Multicentered Short Hydrogen Bond Arrays to Potency of Active Site-Directed Serine Protease Inhibitors

AUTHOR(S): Katz, Bradley A.; Spencer, Jeffrey R.; Elrod, Kyle; Luong, Christine; Mackman, Richard L.; Rice, Mark; Sprengeler, Paul A.; Allen, Darin; Janc, James

CORPORATE SOURCE: Celera, South San Francisco, CA, 94080, USA

SOURCE: Journal of the American Chemical Society (2002), 124(39), 11657-11668
CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We describe and compare the pH dependencies of the potencies and of the bound structures of two inhibitor isosteres that form multicentered short hydrogen bond arrays at the active sites of trypsin, thrombin, and urokinase type plasminogen activator (urokinase or uPA) over certain ranges of pH. Depending on the pH, short hydrogen bond arrays at the active site are mediated by two waters, one in the oxyanion hole (H2Ooxy) and one on the other (S2) side of the inhibitor (H2OS2), by one water (H2Ooxy), or by no water. The dramatic variation in the length of the active site hydrogen bonds as a function of pH, of inhibitor, and of enzyme, along with the involvement or absence of ordered water, produces a large structural manifold of active site hydrogen bond motifs. Diverse examples of multicentered and two-centered short hydrogen bond arrays, both at and away from the active site, recently discovered in several protein crystal systems, suggest that short hydrogen bonds in proteins may be more common than has been recognized. The short hydrogen bond arrays resemble one another with respect to ionic nature, highly polar environment, multitude of assocd. ordinary hydrogen bonds, and disparate pKa values of participating groups. Comparison of structures and Ki values of trypsin complexes at pH values where the multicentered short hydrogen bond arrays

mediating inhibitor binding are present or absent indicate that these arrays have a minor effect on inhibitor potency. These features suggest little covalent nature within the short hydrogen bonds, despite their extraordinary shortness (as short as 2.0 .ANG.).

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 28 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:866569 CAPLUS Full-text
DOCUMENT NUMBER: 136:395308
TITLE: Engineering inhibitors highly selective for the S1 sites of Ser190 trypsin-like serine protease drug targets
AUTHOR(S): Katz, Bradley A.; Sprengeler, Paul A.; Luong, Christine; Verner, Erik; Elrod, Kyle; Kirtley, Matt; Janc, James; Spencer, Jeffrey R.; Breitenbucher, J. Guy; Hui, Hon; McGee, Danny; Allen, Darin; Martelli, Arnold; Mackman, Richard L.
CORPORATE SOURCE: Axys Pharmaceutical Corporation, South San Francisco, CA, 94080, USA
SOURCE: Chemistry & Biology (2001), 8(11), 1107-1121
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Involved or implicated in a wide spectrum of diseases, trypsin-like serine proteases comprise well studied drug targets and anti-targets that can be subdivided into two major classes. In one class there is a serine at position 190 at the S1 site, as in urokinase type plasminogen activator (urokinase or uPA) and factor VIIa, and in the other there is an alanine at 190, as in tissue type plasminogen activator (tPA) and factor Xa. A hydrogen bond unique to Ser190 protease-arylamidine complexes between O.gamma.Ser190 and the inhibitor amidine confers an intrinsic preference for such inhibitors toward Ser190 proteases over Ala190 counterparts. Results: Based on the structural differences between the S1 sites of Ser190 and Ala190 protease-arylamidine complexes, we amplified the selectivity of amidine inhibitors toward uPA and against tPA, by factors as high as 220-fold, by incorporating a halo group ortho to the amidine of a lead inhibitor scaffold. Comparison of Ki values of such halo-substituted and parent inhibitors toward a panel of Ser190 and Ala190 proteases demonstrates pronounced selectivity of the halo analogs for Ser190 proteases over Ala190 counterparts. Crystal structures of Ser190 proteases, uPA and trypsin, and of an Ala190 counterpart, thrombin, bound by a set of ortho (halo, amidino) aryl inhibitors and of non-halo parents reveal the structural basis of the exquisite selectivity and validate the design principle. Conclusions: Remarkable selectivity enhancements of exceptionally small inhibitors are achieved toward the uPA target over the highly similar tPA anti-target through a single atom substitution on an otherwise relatively non-selective scaffold. Overall selectivities for uPA over tPA as high as 980-fold at physiol. pH were realized. The increase in selectivity results from the displacement of a single bound water mol. common to the S1 site of both the uPA target and the tPA anti-target because of the ensuing deficit in hydrogen bonding of the arylamidine inhibitor when bound in the Ala190 protease anti-target.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:628981 CAPLUS Full-text
DOCUMENT NUMBER: 136:47957
TITLE: Optimization of a screening lead for factor VIIa/TF

AUTHOR(S): Young, W. B.; Kolesnikov, A.; Rai, R.; Sprengeler, P. A.; Leahy, E. M.; Shrader, W. D.; Sangalang, J.; Burgess-Henry, J.; Spencer, J.; Elrod, K.; Cregar, L.

CORPORATE SOURCE: Departments of Medicinal Chemistry, Structural Chemistry, and Enzymology, Axys Pharmaceuticals, Inc., South San Francisco, CA, 94080, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(17), 2253-2256
CODEN: BMCLE8; ISSN: 0960-894X

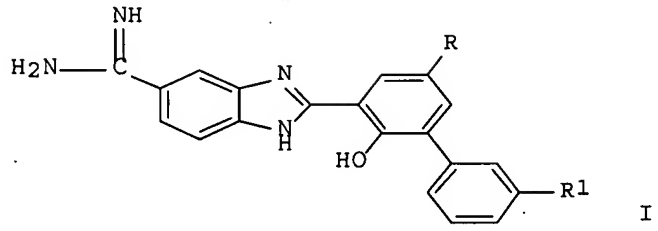
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:47957

GI



I

AB The structure-based design and progression of a screening lead (I, R = Cl, R1 = NH2) to a 3 nM factor VIIa/TF inhibitor I, (R = CH2CO2H, R1 = NO2) with improved selectivity vs. related enzymes is described.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:500142 CAPLUS Full-text

DOCUMENT NUMBER: 135:235905

TITLE: Development of serine protease inhibitors displaying a multicentered short (<2.3 .ANG.) hydrogen bond binding mode: Inhibitors of urokinase-type plasminogen activator and factor Xa

AUTHOR(S): Verner, Erik; Katz, Bradley A.; Spencer, Jeffrey R.; Allen, Darin; Hataye, Jason; Hruzewicz, Witold; Hui, Hon C.; Kolesnikov, Aleksandr; Li, Yong; Luong, Christine; Martelli, Arnold; Radika, Kesavan; Rai, Roopa; She, Miles; Shrader, William; Sprengeler, Paul A.; Trapp, Sean; Wang, Jing; Young, Wendy B.; Mackman, Richard L.

CORPORATE SOURCE: Departments of Medicinal Chemistry Structural Biology and Biochemistry and Enzymology, Axys Pharmaceuticals Inc., South San Francisco, CA, 94080, USA

SOURCE: Journal of Medicinal Chemistry (2001), 44(17), 2753-2771
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Novel scaffolds that bind to serine proteases through a unique network of short hydrogen bonds to the catalytic Ser195 have been developed. The resulting potent serine protease inhibitors were designed from lead mol. 2-(2-hydroxyphenyl)1H-benzoimidazole-5-carboxamidine, 6b, which is known to display several modes of binding. For instance, 6b can recruit zinc and bind in a manner similar to that reported by bis(5-amidino-2- benzimidazolyl)methane (BABIM) (Nature 1998, 391, 608-612). Alternatively, 6b can bind in the absence of zinc through a multicentered network of short (<2.3 .ANG.) hydrogen bonds. The lead structure was optimized in the zinc-independent binding mode toward a panel of six human serine proteases to yield optimized inhibitors such as 2-(3-bromo-2-hydroxy-5-methylphenyl)-1H-indole-5-carboxamidine, 22a, and 2-(2-hydroxybiphenyl-3-yl)-1H-indole-5-carboxamidine, 22f. Structure-activity relationships detd. that, apart from the amidine function, an indole or benzimidazole and an ortho substituted phenol group were also essential components for optimal potency. The affinities (Ki) of 22a and 22f, for example, bearing these groups ranged from 8 to 600 nM toward a panel of six human serine proteases. High-resoln. crystal structures revealed that the binding mode of these mols. in several of the enzymes was identical to that of 6b and involved short (<2.3 .ANG.) hydrogen bonds among the inhibitor hydroxyl oxygen, Ser195, and a water mol. trapped in the oxyanion hole. In summation, novel and potent trypsin-like serine protease inhibitors possessing a unique mode of binding have been discovered.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 31 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:246441 CAPLUS Full-text

DOCUMENT NUMBER: 135:89065

TITLE: A Novel Serine Protease Inhibition Motif Involving a Multi-centered Short Hydrogen Bonding Network at the Active Site

AUTHOR(S): Katz, Bradley A.; Elrod, Kyle; Luong, Christine; Rice, Mark J.; Mackman, Richard L.; Sprengeler, Paul A.; Spencer, Jeffrey; Hataye, Jason; Janc, James; Link, John; Litvak, Joane; Rai, Roopa; Rice, Ken; Sideris, Steve; Verner, Erik; Young, Wendy

CORPORATE SOURCE: Axys Pharmaceuticals Corporation, South San Francisco, CA, 94080, USA

SOURCE: Journal of Molecular Biology (2001), 307(5), 1451-1486
CODEN: JMOBAK; ISSN: 0022-2836

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We describe a new serine protease inhibition motif in which binding is mediated by a cluster of very short hydrogen bonds (<2.3 .ANG.) at the active site. This protease-inhibitor binding paradigm is obsd. at high resoln. in a large set of crystal structures of trypsin, thrombin, and urokinase-type plasminogen activator (uPA) bound with a series of small mol. inhibitors (2-(2-phenol)indoles and 2-(2-phenol)benzimidazoles). In each complex there are eight enzyme-inhibitor or enzyme-water-inhibitor hydrogen bonds at the active site, three of which are very short. These short hydrogen bonds connect a triangle of oxygen atoms comprising O.gamma.Ser195, a water mol. co-bound in the oxyanion hole (H2Ooxy), and the phenolate oxygen atom of the inhibitor (O6'). Two of the other hydrogen bonds between the inhibitor and active site of the trypsin and uPA complexes become short in the thrombin counterparts, extending the three-centered short hydrogen-bonding array into a tetrahedral array of atoms (three oxygen and one nitrogen) involved in short hydrogen bonds. In the uPA complexes, the extensive hydrogen-bonding interactions at the active site prevent the inhibitor S1 amidine from forming direct hydrogen bonds with Asp189 because the S1 site is deeper in uPA than in trypsin or

thrombin. Ionization equil. at the active site assocd. with inhibitor binding are probed through detn. and comparison of structures over a wide range of pH (3.5 to 11.4) of thrombin complexes and of trypsin complexes in three different crystal forms. The high-pH trypsin-inhibitor structures suggest that His57 is protonated at pH values as high as 9.5. The pH-dependent inhibition of trypsin, thrombin, uPA and factor Xa by 2-(2-phenol)benzimidazole analogs in which the pKa of the phenol group is modulated is shown to be consistent with a binding process involving ionization of both the inhibitor and the enzyme. These data further suggest that the pKa of His57 of each protease in the unbound state in soln. is about the same,.apprx.6.8. By comparing inhibition consts. (Ki values), inhibitor solubilities, inhibitor conformational energies and corresponding structures of short and normal hydrogen bond-mediated complexes, we have estd. the contribution of the short hydrogen bond networks to inhibitor affinity (.apprx.1.7 kcal/mol). The structures and Ki values assocd. with the short hydrogen-bonding motif are compared with those corresponding to an alternate, Zn2+-mediated inhibition motif at the active site. Structural differences among apo-enzymes, enzyme-inhibitor and enzyme-inhibitor-Zn2+ complexes are discussed in the context of affinity determinants, selectivity development, and structure-based inhibitor design. (c) 2001 Academic Press.

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 32 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:421114 CAPLUS Full-text

DOCUMENT NUMBER: 133:58803

TITLE: Preparation of 2-arylindole- or -benzimidazolecarboxamidines and analogs as serine protease inhibitors

INVENTOR(S): Allen, Darin Arthur; Hataye, Jason M.; Hruzewicz, Witold N.; Kolesnikov, Aleksandr; Mackman, Richard Laurence; Rai, Roopa; Spencer, Jeffrey R.; Verner, Erik J.; Young, Wendy B.

PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 187 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

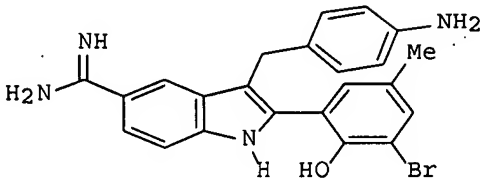
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035886	A2	20000622	WO 1999-US30302	19991217
WO 2000035886	A3	20001026		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2355249	A1	20000622	CA 1999-2355249	19991217
EP 1140859	A2	20011010	EP 1999-968917	19991217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9916363	A	20011211	BR 1999-16363	19991217
HU 200104987	A2	20020729	HU 2001-4987	19991217
EE 200100323	A	20020815	EE 2001-323	19991217

JP 2002532479	T	20021002	JP 2000-588148		19991217
NZ 512375	A	20031128	NZ 1999-512375		19991217
AU 779117	B2	20050106	AU 2000-27115		19991217
TR 200102533	T2	20060621	TR 2001-200102533		19991217
NO 2001002980	A	20010801	NO 2001-2980		20010615
MX 2001PA06070	A	20010911	MX 2001-PA6070		20010615
US 6867200	B1	20050315	US 2002-868276		20020118
PRIORITY APPLN. INFO.:			US 1998-113007P	P	19981218
			WO 1999-US30302	W	19991217

OTHER SOURCE(S): MARPAT 133:58803

GI



I

AB R1Z1Z2R2 [I; R1 = H2NC(:NH), etc.; R2 = halo, OH, CO2H, phenyl(alkyl)oxy, etc.; Z1 = (un)substituted indolylene, -benzimidazolylene, etc.; Z2 = (un)substituted phenylene, pyridinediyl, etc.] were prepd. Thus, 1-(3-bromo-2-hydroxy-5-methylphenyl)-3-(4-nitrophenyl)-1-propanone was condensed with 4-(H2NHN)C6H4C(:NH)NH2 and the product cyclized to give, after redn., title compd. II. Data for biol. activity of I were given.

L8 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:184240 CAPLUS Full-text

DOCUMENT NUMBER: 130:209707

TITLE: Preparation of 2-substituted phenyl-benzimidazole antibacterial agents

INVENTOR(S): Ohemeng, Kwasi Adomako; Nguyen, Van Nhatton

PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA

SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

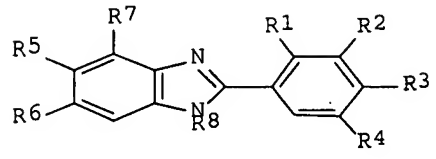
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911627	A1	19990311	WO 1998-US18586	19980904
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 5942532	A	19990824	US 1997-924558	19970905
AU 9893054	A	19990322	AU 1998-93054	19980904

PRIORITY APPLN. INFO.: US 1997-924558 A 19970905
WO 1998-US18586 W 19980904

OTHER SOURCE(S): MARPAT 130:209707
GI



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AB Benzimidazoles I [R1 = H, OH, alkoxy; R2, R3, R4 = H, OH, alkyl, CF3, halo, etc.; R5 = H, amino, amidino; R6 = nitro, C(NHR9):NR10; R7 = H, amino, nitro; R8 = H, Me], antibacterial compds., were prepd. These compds. are effective in inhibiting the action of a bacterial histidine protein kinase and are useful as anti-infective agents against a variety of bacterial organisms, including organisms which are resistant to other known antibiotics. E.g., 3,4-diaminobenzimidate, prepd. from 3,4-diaminobenzonitrile, was treated with NH3/EtOH, then with 4-Me3CC6H4CHO to give 2-[4-(1,1-dimethylethyl)phenyl]-2H-benzimidazole-5- carboximidamide.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 20-33

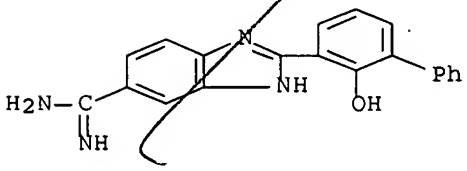
L8 ANSWER 20 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:339493 CAPLUS Full-text
DOCUMENT NUMBER: 141:116428
TITLE: 3D-QSAR CoMFA/CoMSIA studies on urokinase plasminogen activator (uPA) inhibitors: a strategic design in novel anticancer agents
AUTHOR(S): Bhongade, B. A.; Gadad, A. K.
CORPORATE SOURCE: College of Pharmacy, Department of Medicinal Chemistry, J. N. Medical College, Belgaum, 590010, India
SOURCE: Bioorganic & Medicinal Chemistry (2004), 12(10), 2797-2805
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Comparative mol. field anal. (CoMFA) and comparative mol. similarity indexes anal. (CoMSIA) was performed on a series of indole/benzoimidazole- 5-carboxamidines as urokinase plasminogen activator (uPA) inhibitors. The ligand mol. superimposition on template structure was performed by atom/shape-based RMS fit, multifit, and RMSD fit methods. The removal of two outliers from the initial training set of 30 mols. improved the predictivity of the models. The statistically significant model was established from 28 mols., which were validated by evaluation of test set of nine compds. The atom-based RMS alignment yielded best predictive CoMFA model (r2cv=0.611, r2cnv=0.778, F value=43.825, r2bs=0.842, r2pred=0.616 with two components) while the CoMSIA model yielded (r2cv=0.499, r2cnv=0.976, F value=96.36, r2bs=0.993, r2pred=0.694 with eight components). The contour maps obtained from 3D-QSAR studies were appraised for the activity trends of the mols. analyzed. The

results indicate that the steric, electrostatic, and hydrogen bond donor/acceptor substituents play significant role in uPA activity and selectivity of these compds. The data generated from the present study can be used as putative pharmacophore in the design of novel, potent, and selective urokinase plasminogen activator inhibitors as cancer therapeutics.

IT 277311-06-5
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(3D-QSAR CoMFA/CoMSIA studies on urokinase plasminogen activator (uPA) inhibitors as novel anticancer agents)

RN 277311-06-5 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:991295 CAPLUS Full-text
DOCUMENT NUMBER: 140:35966
TITLE: Amidine derivatives for treating amyloidosis and neurodegenerative diseases
INVENTOR(S): Chalifour, Robert J.; Kong, Xianqi; Wu, Xinfu; Lu, Wenshuo; Tidwell, Richard R.; Boykin, David
PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA; Georgia State University Research Foundation, Inc.
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003103598	A2	20031218	WO 2003-US17992	20030609
WO 2003103598	A3	20060309		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2488493	A1	20031218	CA 2003-2488493	20030609
AU 2003251418	A1	20031222	AU 2003-251418	20030609
EP 1572129	A2	20050914	EP 2003-757414	20030609

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

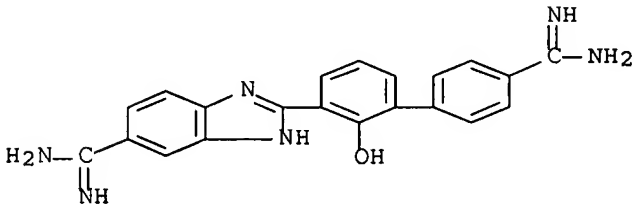
JP 2006501160	T	20060112	JP 2004-510719		20030609
US 2004147531	A1	20040729	US 2003-731463		20031205
US 2007021483	A1	20070125	US 2006-335171		20060119
PRIORITY APPLN. INFO.:			US 2002-387001P	P	20020607
			US 2001-316761P	P	20010831
			US 2002-234643	A1	20020903
			WO 2003-US17992	W	20030609
			US 2003-731463	B1	20031205

AB The present invention relates to the use of amidine compds. in the treatment of amyloid related diseases. In particular, the invention relates to a method of treating or preventing an amyloid-related disease in a subject comprising administering to the subject a therapeutic amt. of an amidine compd. Among the compds. for use according to the invention are those according to the following Formulas, such that, when administered, amyloid fibril formation, neurodegeneration, or cellular toxicity is reduced or inhibited.

IT 500714-98-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of amidine derivs. for treating amyloidosis and neurodegenerative diseases)

RN 500714-98-7 CAPLUS

CN 1H-Benzimidazole-5-carboximidamide, 2-[4'-(aminoiminomethyl)-2-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



L8 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2003:656754 CAPLUS Full-text
DOCUMENT NUMBER:	139:197482
TITLE:	Preparation of 2-[5-(5-carbamimidoyl-1H-heteroaryl)]-6-hydroxybiphenyl derivatives as factor VIIa inhibitors
INVENTOR(S):	Kolesnikov, Aleksandr; Rai, Roopa; Shrader, William Dvorak; Young, Wendy B.
PATENT ASSIGNEE(S):	Axys Pharmaceuticals, Inc., USA
SOURCE:	PCT Int. Appl., 68 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068756	A1	20030821	WO 2003-US4081	20030212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2474195	A1	20030821	CA 2003-2474195		20030212
AU 2003215158	A1	20030904	AU 2003-215158		20030212
EP 1474400	A1	20041110	EP 2003-710972		20030212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005523279	T	20050804	JP 2003-567887		20030212
US 2005203094	A1	20050915	US 2005-504119		20050505
PRIORITY APPLN. INFO.:			US 2002-356473P	P	20020213
			US 2003-439043P	P	20030108
			WO 2003-US4081	W	20030212

OTHER SOURCE(S): MARPAT 139:197482
GI

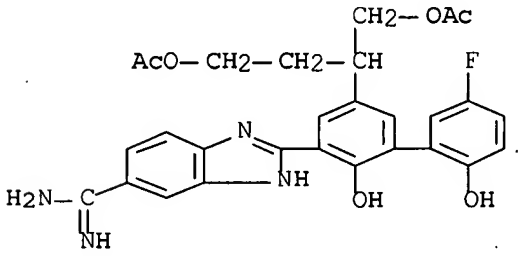
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X1-X4 = N, (un)substituted CH; R1, R2 = H, alkyl, hydroxyalkyl, halogen; R3 = (un)substituted hydroxyalkyl, carboxyalkyl, carboxycycloalkyl, carboxyalkoxy, dicarboxyalkoxy, lactam; R4 = (un)substituted Ph; Y = H, OH, (un)substituted alkoxy, CO2H] were prepd. as inhibitors of factor VIIa and Xa (no data). Thus, the benzimidazole II was prepd. from 4-HOC6H4CH:C(CO2Me)2 and 3,4-(H2N)2C6H3C(:NH)NH2.HCl in 9 steps.

IT 583032-11-5P 583032-13-7P 583032-14-8P
583032-16-0P 583032-19-3P 583032-21-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 2-[5-(5-carbamimidoyl-1H-heteroaryl)]-6-hydroxybiphenyl derivs. as factor VIIa inhibitors)

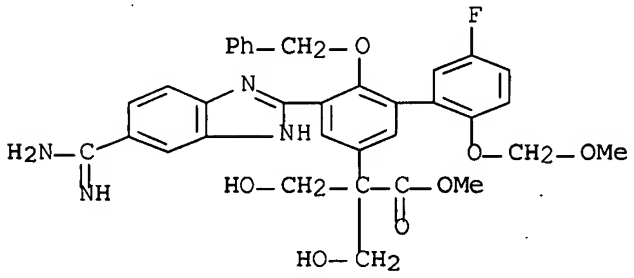
RN 583032-11-5 CAPLUS

CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[3-(acetyloxy)-1-[(acetyloxy)methyl]propyl]-5'-fluoro-2,2'-dihydroxy[1,1'-biphenyl]-3-yl]-, hydrochloride (3:4) (9CI) (CA INDEX NAME)

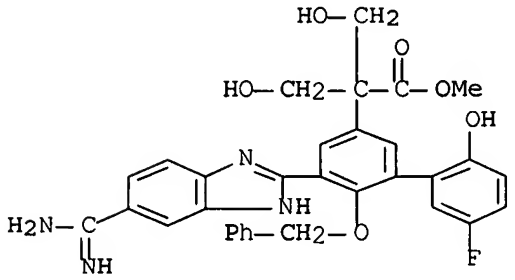


●4/3 HCl

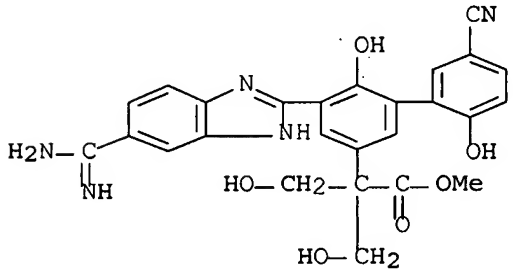
RN 583032-13-7 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-.alpha.,.alpha.-bis(hydroxymethyl)-2'-(methoxymethoxy)-6-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)



RN 583032-14-8 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2'-hydroxy-.alpha.,.alpha.-bis(hydroxymethyl)-6-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)

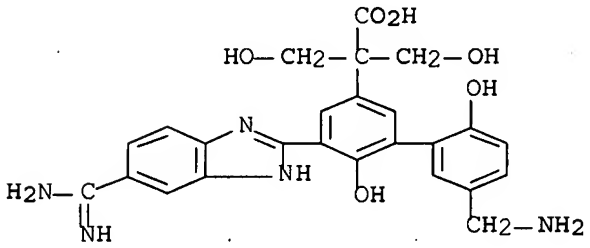


RN 583032-16-0 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-cyano-2',6-dihydroxy-.alpha.,.alpha.-bis(hydroxymethyl)-, methyl ester (9CI) (CA INDEX NAME)

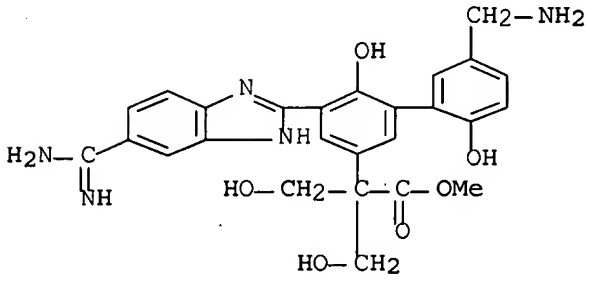


RN 583032-19-3 CAPLUS

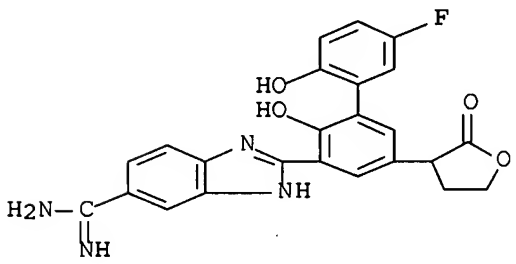
CN [1,1'-Biphenyl]-3-acetic acid, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-(aminomethyl)-2',6-dihydroxy-.alpha.,.alpha.-bis(hydroxymethyl)- (9CI) (CA INDEX NAME)



RN 583032-21-7 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-(aminomethyl)-2',6-dihydroxy-.alpha.,.alpha.-bis(hydroxymethyl)-, methyl ester (9CI) (CA INDEX NAME)

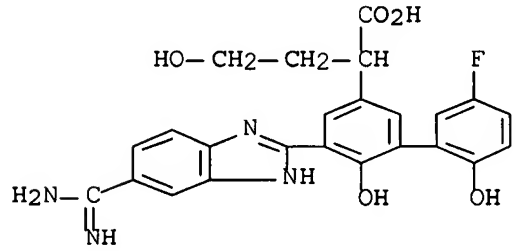


IT 583032-09-1P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 2-[5-(5-carbamimidoyl-1H-heteroaryl)]-6-hydroxybiphenyl derivs. as factor VIIa inhibitors)
RN 583032-09-1 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5'-fluoro-2,2'-dihydroxy-5-(tetrahydro-2-oxo-3-furanyl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)

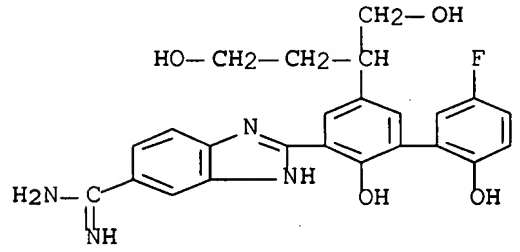


IT 583032-10-4P 583032-12-6P 583032-15-9P
583032-18-2P 583032-20-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-[5-(5-carbamimidoyl-1H-heteroaryl)]-6-hydroxybiphenyl derivs. as factor VIIa inhibitors)

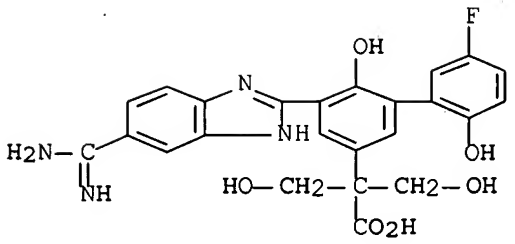
RN 583032-10-4 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy-.alpha.-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



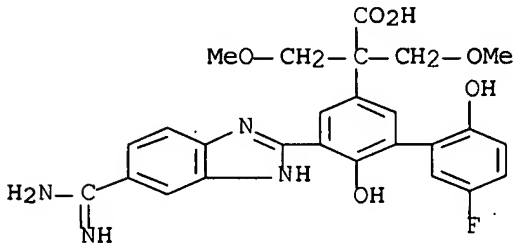
RN 583032-12-6 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5'-fluoro-2,2'-dihydroxy-5-[3-hydroxy-1-(hydroxymethyl)propyl][1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



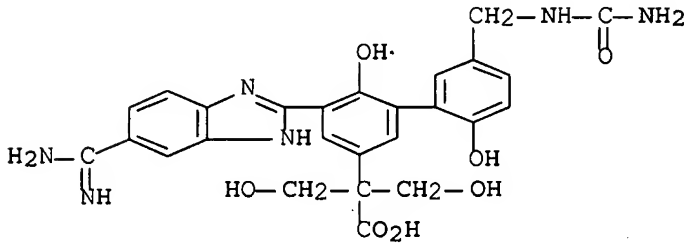
RN 583032-15-9 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy-.alpha.,.alpha.-bis(hydroxymethyl)- (9CI) (CA INDEX NAME)



RN 583032-18-2 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy-.alpha.,.alpha.-bis(methoxymethyl)- (9CI) (CA INDEX NAME)



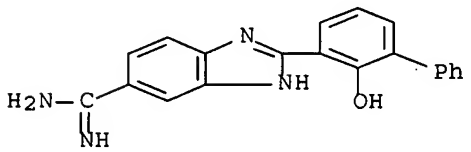
RN 583032-20-6 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5'-[[(aminocarbonyl)amino]methyl]-5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy-.alpha.,.alpha.-bis(hydroxymethyl)- (9CI) (CA INDEX NAME)



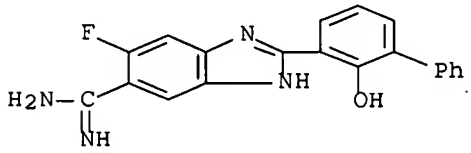
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 23 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:343069 CAPLUS Full-text
DOCUMENT NUMBER: 139:226287
TITLE: Elaborate Manifold of Short Hydrogen Bond Arrays Mediating Binding of Active Site-directed Serine Protease Inhibitors
AUTHOR(S): Katz, Bradley A.; Elrod, Kyle; Verner, Erik; Mackman,

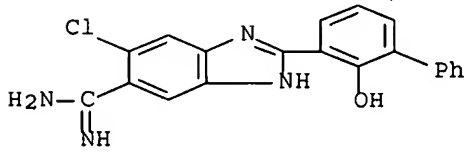
Richard L.; Luong, Christine; Shrader, William D.; Sendzik, Martin; Spencer, Jeffrey R.; Sprengeler, Paul A.; Kolesnikov, Aleks; Tai, Vincent W.-F.; Hui, Hon C.; Guy Breitenbucher, J.; Allen, Darin; Janc, James W.
CORPORATE SOURCE: Celera, South San Francisco, CA, 94080, USA
SOURCE: Journal of Molecular Biology (2003), 329(1), 93-120
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An extensive structural manifold of short hydrogen bond-mediated, active site-directed, serine protease inhibition motifs is revealed in a set of over 300 crystal structures involving a large suite of small mol. inhibitors (2-(2-phenol)-indoles and 2-(2-phenol)-benzimidazoles) detd. over a wide range of pH (3.5-11.4). The active site hydrogen-bonding mode was found to vary markedly with pH, with the steric and electronic properties of the inhibitor, and with the type of protease (trypsin, thrombin or urokinase type plasminogen activator (uPA)). The pH dependence of the active site hydrogen-bonding motif is often intricate, constituting a distinct fingerprint of each complex. Isosteric replacements or minor substitutions within the inhibitor that modulate the pKa of the phenol hydroxyl involved in short hydrogen bonding, or that affect steric interactions distal to the active site, can significantly shift the pH-dependent structural profile characteristic of the parent scaffold, or produce active site-binding motifs unique to the bound analog. Ionization equil. at the active site assocd. with inhibitor binding are probed in a series of the protease-inhibitor complexes through anal. of the pH dependence of the structure and environment of the active site-binding groups involved in short hydrogen bond arrays. Structures detd. at high pH (>11), suggest that the pKa of His57 is dramatically elevated, to a value as high as .apprx.11 in certain complexes. Ki values involving uPA and trypsin detd. as a function of pH for a set of inhibitors show pronounced parabolic pH dependence, the pH for optimal inhibition governed by the pKa of the inhibitor phenol involved in short hydrogen bonds. Comparison of structures of trypsin, thrombin and uPA, each bound by the same inhibitor, highlights important structural variations in the S1 and active sites accessible for engineering notable selectivity into remarkably small mols. with low nanomolar Ki values.
IT 277311-06-5D, CRA 7806, complexes with serine protease
430476-32-7, CRA 10818 430476-35-0D, CRA 10762,
complexes with serine protease 593267-27-7, CRA 16935
593267-28-8, CRA 17312 593267-36-8D, CRA 23653,
complexes with serine protease
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(elaborate manifold of short hydrogen bond arrays mediating binding of active site-directed serine protease inhibitors to trypsin, thrombin and urokinase type plasminogen activator)
RN 277311-06-5 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)-(9CI) (CA INDEX NAME)



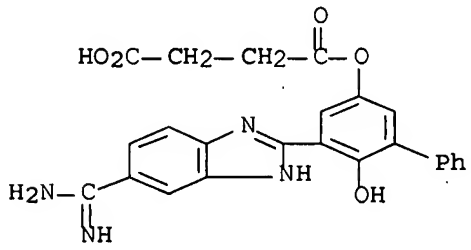
RN 430476-32-7 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 6-fluoro-2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



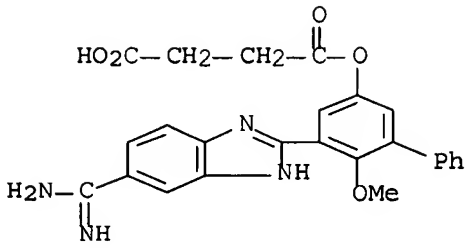
RN 430476-35-0 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 6-chloro-2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



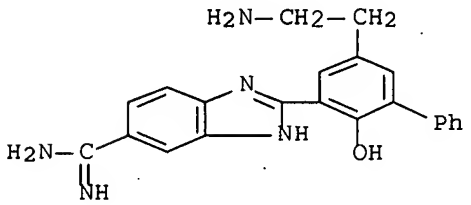
RN 593267-27-7 CAPLUS
CN Butanedioic acid, mono[5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy[1,1'-biphenyl]-3-yl] ester (9CI) (CA INDEX NAME)



RN 593267-28-8 CAPLUS
CN Butanedioic acid, mono[5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-methoxy[1,1'-biphenyl]-3-yl] ester (9CI) (CA INDEX NAME)



RN 593267-36-8 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-(2-aminoethyl)-2-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:173414 CAPLUS Full-text
DOCUMENT NUMBER: 138:215350
TITLE: Amidine derivatives for treating amyloid-related diseases
INVENTOR(S): Chalifour, Robert J.; Kong, Xianqi; Wu, Xinfu; Lu, Wenshuo
PATENT ASSIGNEE(S): Neurochem Inc., Can.
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003017994	A1	20030306	WO 2002-CA1353	20020903

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2455497	A1	20030306	CA 2002-2455497		20020903
AU 2002325117	A1	20030310	AU 2002-325117		20020903
US 2004006092	A1	20040108	US 2002-234643		20020903
EP 1420773	A1	20040526	EP 2002-758012		20020903
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
BR 2002012078	A	20040928	BR 2002-12078		20020903
JP 2005504053	T	20050210	JP 2003-522514		20020903
CN 1658852	A	20050824	CN 2002-815770		20020903
US 2004147531	A1	20040729	US 2003-731463		20031205
IN 2004CN00219	A	20051209	IN 2004-CN219		20040203
NO 2004000497	A	20040414	NO 2004-497		20040204
MX 2004PA01153	A	20050217	MX 2004-PA1153		20040206
US 2007021483	A1	20070125	US 2006-335171		20060119
PRIORITY APPLN. INFO.:			US 2001-316761P	P	20010831
			US 2002-387001P	P	20020607
			US 2002-234643	A1	20020903
			WO 2002-CA1353	W	20020903
			US 2003-731463	B1	20031205

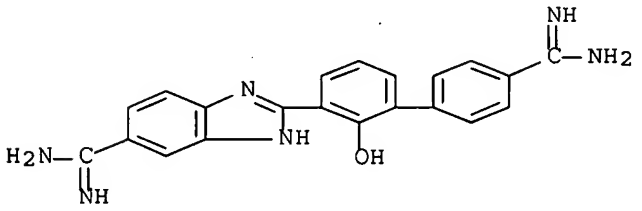
OTHER SOURCE(S): MARPAT 138:215350

AB The invention discloses the use of amidine compds. in the treatment of amyloid-related diseases (e.g. Alzheimer's disease, Down's syndrome, type II diabetes). In particular, the invention discloses a method for treating or preventing an amyloid-related disease in a subject comprising administering to the subject a therapeutic amt. of an amidine compd. The compds. of the invention (Markush included) are such that, when administered, reduce or inhibit amyloid fibril formation, neurodegeneration, or cellular toxicity. Compd. prepn. is described.

IT 500714-98-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amidine derivs. for treating amyloid-related diseases)

RN 500714-98-7 CAPLUS

CN 1H-Benzimidazole-5-carboximidamide, 2-[4'-(aminoiminomethyl)-2-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:58259 CAPLUS Full-text

DOCUMENT NUMBER: 138:117652

TITLE: 2-[5-(5-carbamimidoyl-1H-heteroaryl)-6-hydroxybiphenyl-3-yl]succinic acid derivatives as factor VIIa inhibitors

INVENTOR(S): Hu, Huiyong; Kolesnikov, Aleksandr; Sperandio, David; Young, Wendy Beth; Shrader, William Dvorak

PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003006670	A2	20030123	WO 2002-US21340	20020703
WO 2003006670	A3	20030522		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002313655	A1	20030129	AU 2002-313655	20020703
US 2003114457	A1	20030619	US 2002-190147	20020703
US 2005176797	A1	20050811	US 2004-940001	20040913
PRIORITY APPLN. INFO.:			US 2001-303953P P	20010709
			US 2002-351054P P	20020122
			US 2002-190147 A1	20020703
			WO 2002-US21340 W	20020703

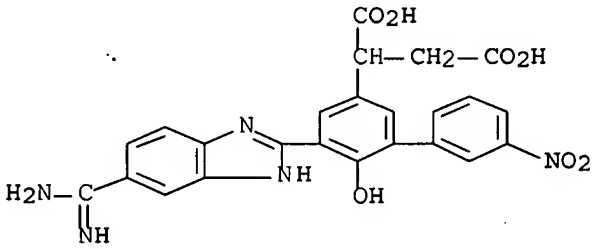
OTHER SOURCE(S): MARPAT 138:117652

AB The present invention relates to derivs. of 2-[5-(5-carbamimidoyl-1H-heteroaryl)-6-hydroxybiphenyl-3-yl]succinic acid as inhibitors of Factors VIIa, IXa, Xa, XIa, in particular Factor VIIa, pharmaceutical compns. comprising these inhibitors, and methods for using these inhibitors for treating or preventing thromboembolic disorders. For example, 2-[5-(5-carbamimidoyl-1H-benzoimidazol-2-yl)-6-hydroxy-3'-nitro-biphenyl-3- yl]-succinic acid was prepd. by reaction of 2-(5-formyl-6-hydroxy-3'-nitro-biphenyl-3-yl)-succinic acid (0.3 g) and 3,4-diaminobenzamidine monohydrochloride (0.17 g) in a yield of 63%.

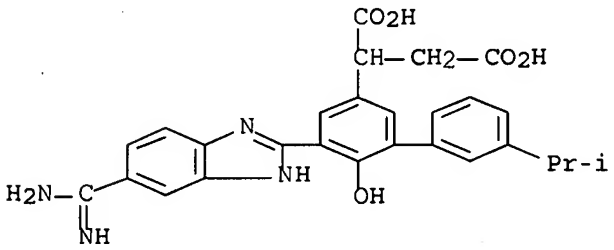
IT 488713-35-5P 488791-78-2P 488791-79-3P
488791-80-6P 488791-81-7P 488791-82-8P
488791-83-9P 488791-85-1P 488791-86-2P
488791-87-3P 488791-88-4P 488791-89-5P
488791-91-9P 488791-92-0P 488791-93-1P
488791-94-2P 488791-95-3P 488791-96-4P
488791-98-6P 488791-99-7P 488792-00-3P
488792-01-4P 488792-02-5P 488792-05-8P
488792-06-9P 488792-07-0P 488792-08-1P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of succinic acid derivs. as anticoagulants)

RN 488713-35-5 CAPLUS

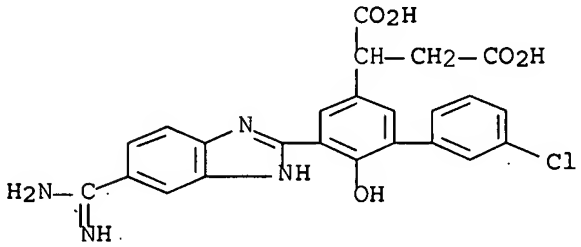
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-3'-nitro[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



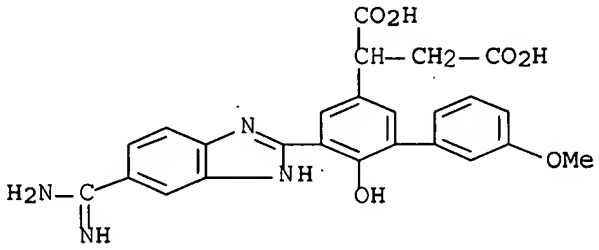
RN 488791-78-2 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-3'-(1-methylethyl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



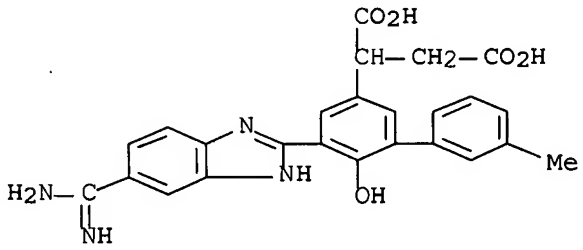
RN 488791-79-3 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-3'-chloro-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



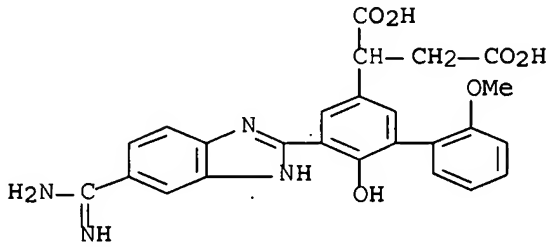
RN 488791-80-6 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-3'-methoxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



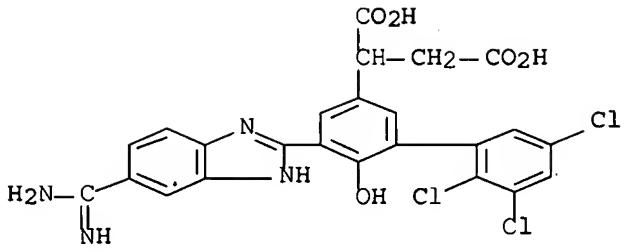
RN 488791-81-7 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-3'-methyl[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



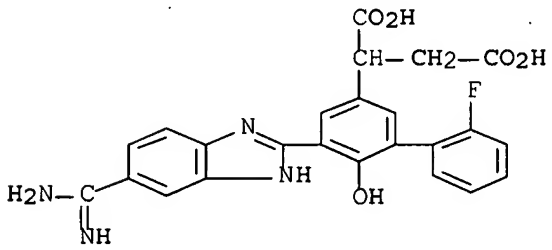
RN 488791-82-8 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-2'-methoxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



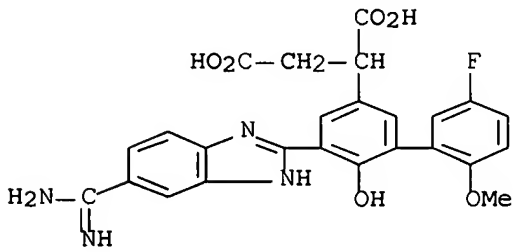
RN 488791-83-9 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',3',5'-trichloro-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



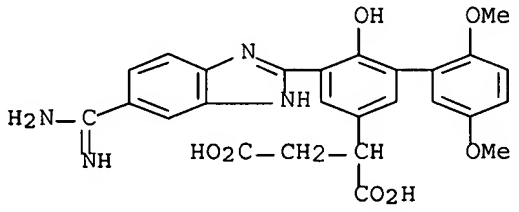
RN 488791-85-1 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2'-fluoro-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



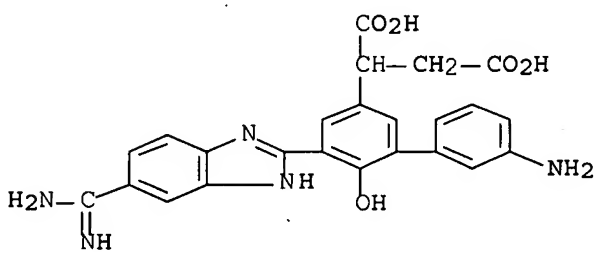
RN 488791-86-2 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-6-hydroxy-2'-methoxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



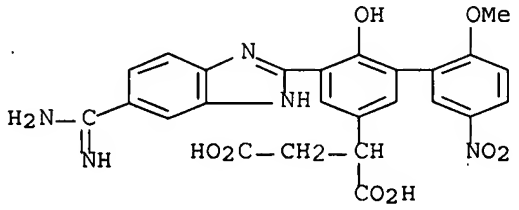
RN 488791-87-3 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-2',5'-dimethoxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



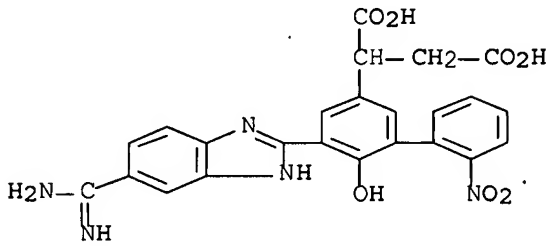
RN 488791-88-4 CAPLUS
CN Butanedioic acid, [3'-amino-5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



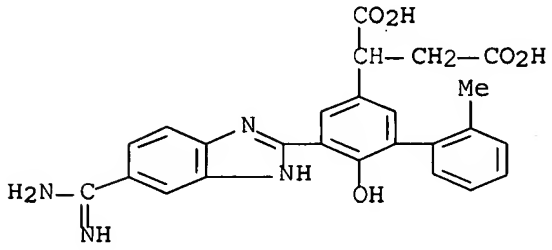
RN 488791-89-5 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-2'-methoxy-5'-nitro[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



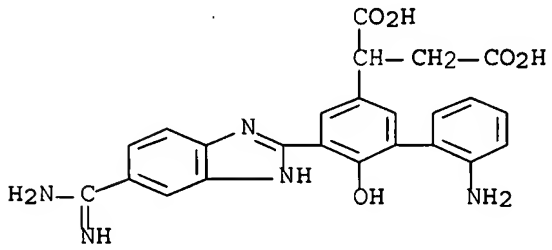
RN 488791-91-9 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-2'-nitro[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



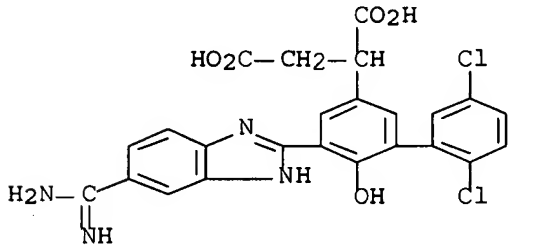
RN 488791-92-0 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-2'-methyl[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



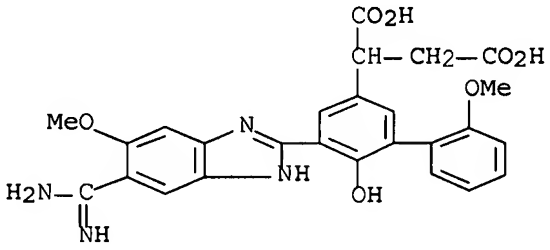
RN 488791-93-1 CAPLUS
CN Butanedioic acid, [2'-amino-5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



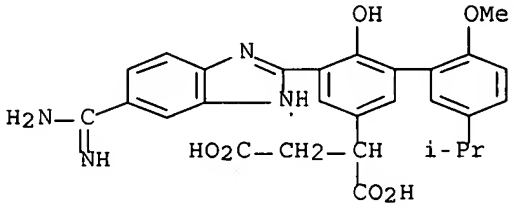
RN 488791-94-2 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',5'-dichloro-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



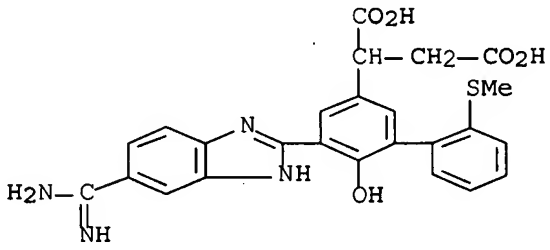
RN 488791-95-3 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-5-methoxy-1H-benzimidazol-2-yl]-6-hydroxy-2'-methoxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



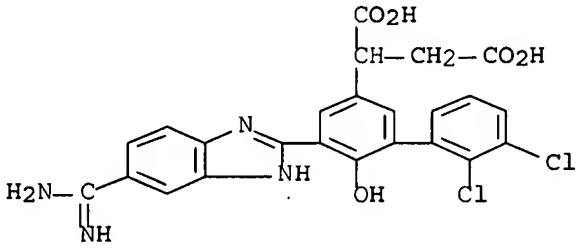
RN 488791-96-4 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-2'-methoxy-5'-(1-methylethyl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



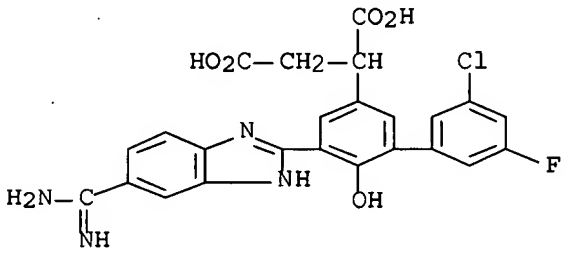
RN 488791-98-6 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-2'-(methylthio)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



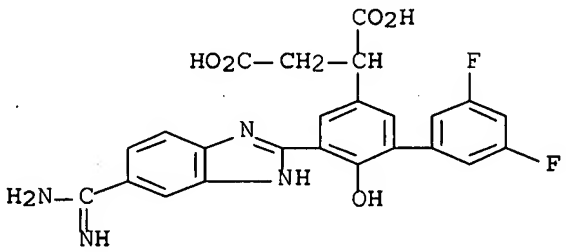
RN 488791-99-7 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',3'-dichloro-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



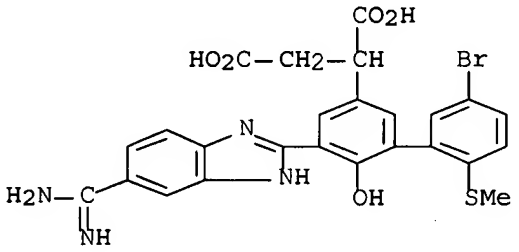
RN 488792-00-3 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-3'-chloro-5'-fluoro-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



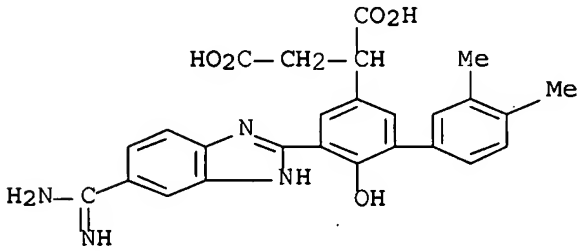
RN 488792-01-4 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-3',5'-difluoro-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



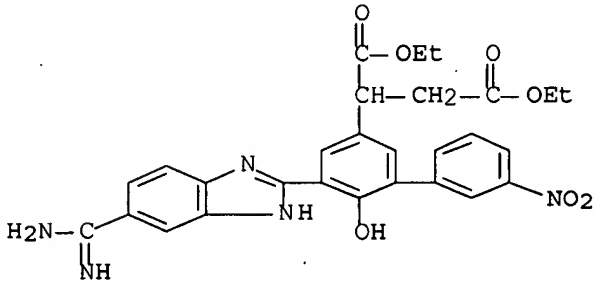
RN 488792-02-5 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-bromo-6-hydroxy-2'-(methylthio)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



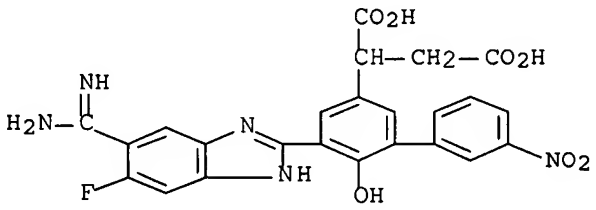
RN 488792-05-8 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-3',4'-dimethyl[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



RN 488792-06-9 CAPLUS
CN Butanedioic acid, [5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-3'-nitro[1,1'-biphenyl]-3-yl]-, diethyl ester (9CI) (CA INDEX NAME)

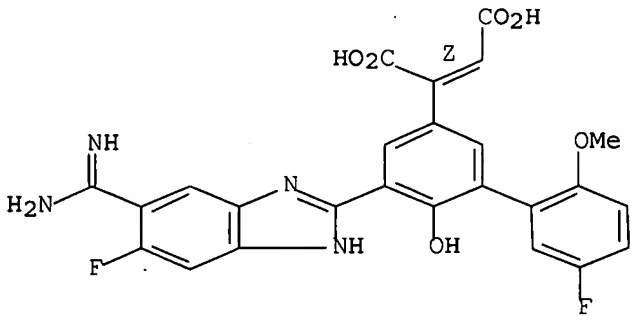


RN 488792-07-0 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-6-fluoro-1H-benzimidazol-2-yl]-6-hydroxy-3'-nitro[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



RN 488792-08-1 CAPLUS
CN 2-Butenedioic acid, 2-[5-[5-(aminoiminomethyl)-6-fluoro-1H-benzimidazol-2-yl]-5'-fluoro-6-hydroxy-2'-methoxy[1,1'-biphenyl]-3-yl]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L8 ANSWER 26 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:57897 CAPLUS Full-text
DOCUMENT NUMBER: 138:122645
TITLE: Preparation of 2-[5-(5-Carbamimidoyl-1H-heteroaryl)-6-hydroxybiphenyl-3-yl]-succinic acid derivatives as factor VIIa inhibitors
INVENTOR(S): Hu, Huiyong; Kolesnikov, Aleksandr; Rai, Roopa; Shrader, William Dvorak; Young, Wendy Beth; Sperandio, David; Hendrix, John; Torkelson, Steve
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003006011	A1	20030123	WO 2002-US21334	20020703

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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US 2003114457	A1	20030619	US 2002-190147		20020703
EP 1408963	A1	20040421	EP 2002-746886		20020703
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PRIORITY APPLN. INFO.:			US 2001-303953P	P	20010709
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OTHER SOURCE(S): MARPAT 138:122645

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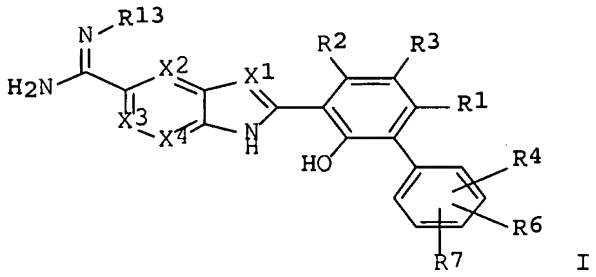


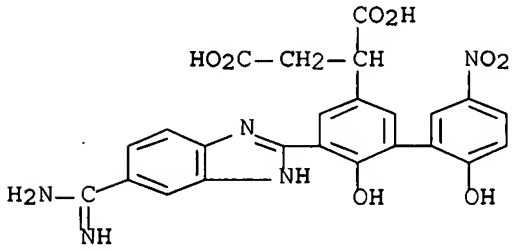
I

AB The present invention relates to [I; X1-X4 = N, CR5 (wherein R5 = H, alkyl); provided that not more than three of X1-X4 are N; R1, R2 = H, alkyl, halo; R3 = CO2R9, -(alkylene)-CO2R9, CR8(CO2R11)alkylene-CO2R9, -C(R8)[(alkylene)nCO2R9]CH(R10)CO2R11 (wherein R8 = H, alkyl, HO; R10 = H, alkyl; R8 and R10 together forms a covalent bond; R9, R11 = H, alkyl, haloalkyl, aryl, aralkyl); R4 = H, alkyl, alkylthio, halo, HO, hydroxyalkyl, alkoxy, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, NO2; R6 = H, alkyl, halo; R7 = H, alkyl, cycloalkyl, alkylthio, halo, HO, NO2, cyano, alkoxy, haloalkoxy, CO2H, alkoxycarbonyl, acylamino, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, etc.; R13 = H, HO, C1-10 alkoxy, COR35 (wherein R35 = alkyl, aryl, haloalkyl, cyanoalkyl, alkoxycarbonyl, hydroxyalkoxycarbonyl, acyloxycarbonyl, haloalkoxycarbonyl)] and individual isomers, mixts. of isomers, or pharmaceutically acceptable salts thereof which are novel inhibitors of factors VIIa, IXa, Xa, XIa, in particular factor VIIa (no data). Also disclosed are pharmaceutical compns. contg. the compds. I for treating or preventing a disease mediated by factor VIIa, in particular thromboembolic disorders. Also claimed is a method for inhibiting coagulation of a biol. sample. Thus, A mixt. of 0.3 g 2-(5-formyl-6-hydroxy-3'-nitrobiphenyl-3- yl)succinic acid, 0.17 g, 3,4-diaminobenzamidine monohydrochloride, and 0.097 g benzoquinone in 50 mL ethanol was heated for approx. 4 h to give, after purifn. by reverse phase HPLC (gradient, acetonitrile/0.02 N aq. HCl) to give 63% 2-[5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-6-hydroxy-3'-nitrobiphenyl-3-yl]succinic acid.

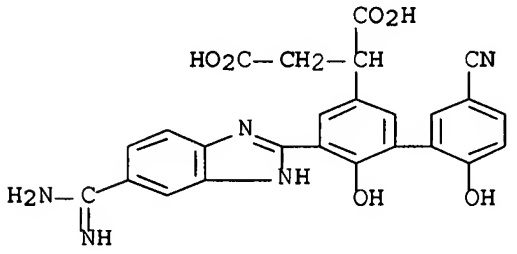
IT 488713-49-1P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-nitrobiphenyl-3-yl]succinic acid 488713-52-6P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-cyano-6,2'-

dihydroxybiphenyl-3-yl]succinic acid 488713-75-3P,
2-[5'-Amino-5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-
dihydroxybiphenyl-3-yl]succinic acid
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); RACT (Reactant or reagent); USES (Uses)
(intermediate; prepn. of [(carbamimidoyl-1H-
heteroaryl)hydroxybiphenylyl]succinic acid derivs. as factor VIIa
inhibitors for treating thromboembolic disorders)

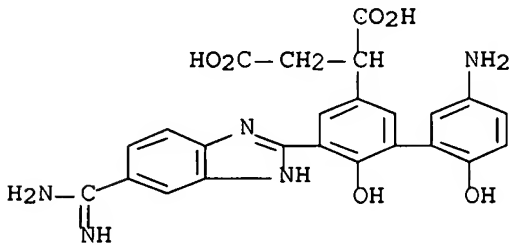
RN 488713-49-1 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-
dihydroxy-5'-nitro[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



RN 488713-52-6 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-cyano-
2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



RN 488713-75-3 CAPLUS
CN Butanedioic acid, [5'-amino-5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-
2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)

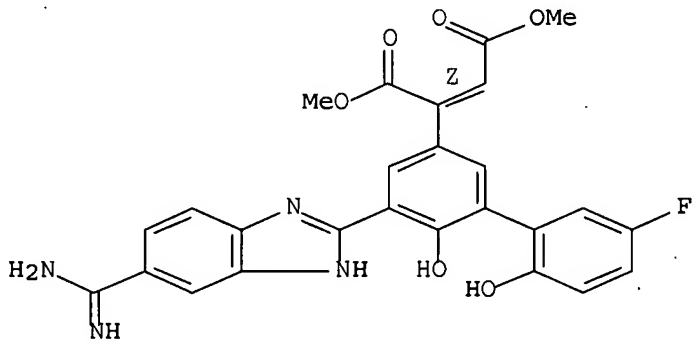


IT 488713-66-2P, (Z)-2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]but-2-enedioic acid dimethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of [(carbamimidoyl-1H-heteroaryl)hydroxybiphenylyl]succinic acid derivs. as factor VIIa inhibitors for treating thromboembolic disorders)

RN 488713-66-2 CAPLUS

CN 2-Butenedioic acid, 2-[5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-, dimethyl ester, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



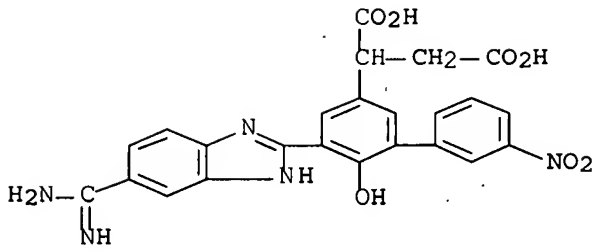
IT 488713-35-5P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6-hydroxy-3'-nitrobiphenyl-3-yl]succinic acid 488713-36-6P, 2-[3'-Acetyl-5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-6-hydroxybiphenyl-3-yl]succinic acid 488713-37-7P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-3'-(1,1-difluoromethoxy)-6-hydroxybiphenyl-3-yl]succinic acid 488713-38-8P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,3'-dihydroxybiphenyl-3-yl]succinic acid 488713-39-9P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-dihydroxybiphenyl-3-yl]succinic acid 488713-40-2P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-3'-aminocarbonyl-6-hydroxybiphenyl-3-yl]succinic acid 488713-41-3P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-3'-cyano-6-hydroxybiphenyl-3-yl]succinic acid 488713-42-4P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]succinic acid 488713-43-5P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-chloro-6,2'-dihydroxybiphenyl-3-yl]succinic acid 488713-44-6P, 2-[5-(5-Carbamimidoyl-6-fluoro-1H-benzimidazol-2-yl)-6,2'-dihydroxybiphenyl-3-yl]succinic acid 488713-45-7P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6-hydroxy-2'-hydroxymethylbiphenyl-3-yl]succinic acid 488713-46-8P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-carboxy-6,2'-dihydroxybiphenyl-3-yl]succinic acid 488713-47-9P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2',5'-trihydroxybiphenyl-3-yl]succinic acid 488713-48-0P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2',6'-trihydroxybiphenyl-3-yl]succinic acid 488713-50-4P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-2'-cyano-6-hydroxybiphenyl-3-yl]succinic acid 488713-51-5P, 2-[5-(6-Carbamimidoyl-1H-benzimidazol-2-yl)-6-hydroxy-3'-

hydroxymethylbiphenyl-3-yl]succinic acid 488713-53-7P,
2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-aminocarbonyl-6-hydroxy-2'-
methoxybiphenyl-3-yl]succinic acid 488713-54-8P,
2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-cyano-6-hydroxy-2'-
methoxybiphenyl-3-yl]succinic acid 488713-55-9P,
2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-aminocarbonyl-6,2'-
dihydroxybiphenyl-3-yl]succinic acid 488713-68-4P,
2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-cyano-6,2'-
dihydroxybiphenyl-3-yl]succinic acid hydrochloride 488713-69-5P,
2-[3'-Aminosulfonyl-5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-6-
hydroxybiphenyl-3-yl]succinic acid 488713-70-8P,
2-[5'-Aminocarbonyl-5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-
dihydroxybiphenyl-3-yl]succinic acid hydrochloride 488713-71-9P,
2-[5'-Aminomethyl-5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-
dihydroxybiphenyl-3-yl]succinic acid 488713-72-0P,
2-[5'-Aminomethyl-5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-
dihydroxybiphenyl-3-yl]succinic acid dihydrochloride 488713-73-1P
, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-
ureidomethylbiphenyl-3-yl]succinic acid 488713-74-2P,
2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-
ureidomethylbiphenyl-3-yl]succinic acid hydrochloride 488713-84-4P
, 1-Ethyl 2-[5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-2',6-dihydroxy-5'-
fluorobiphenyl-3-yl]succinate 488713-85-5P 488713-87-7P
488713-88-8P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-(2-
cyanoethyl)-2',6-dihydroxybiphenyl-3-yl]succinic acid 488713-90-2P
, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-3'-bromo-5'-(cyanomethyl)-
2',6-dihydroxybiphenyl-3-yl]succinic acid 488713-92-4P,
2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-2',6-dihydroxy-5'-(4-
methylpiperazin-1-ylmethyl)biphenyl-3-yl]succinic acid
488713-96-8P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-2',6-
dihydroxy-5'-(hydroxymethyl)biphenyl-3-yl]succinic acid
488714-05-2P, 2-[3'-Bromo-5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-
6,2',6'-trihydroxybiphenyl-3-yl]succinic acid 488714-06-3P,
2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-
methylsulfonylaminobiphenyl-3-yl]succinic acid 488714-07-4P,
2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-
isopropylbiphenyl-3-yl]succinic acid 488714-08-5P,
2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-imidazol-2-
ylbiphenyl-3-yl]succinic acid 488714-09-6P 488714-10-9P
488714-11-0P, 2-[3'-Bromo-5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-
5'-carboxymethyl-6,2'-dihydroxybiphenyl-3-yl]succinic acid
488714-12-1P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-(2-
carboxyethyl)-6,2'-dihydroxybiphenyl-3-yl]succinic acid
488714-13-2P, 2-[2'-Acetyl-5-(5-carbamimidoyl-1H-benzimidazol-2-
yl)-6-hydroxybiphenyl-3-yl]succinic acid 488714-14-3P,
2-[3'-Bromo-5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-
aminocarbonylmethylbiphenyl-3-yl]succinic acid 488714-15-4P,
2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-3',5'-dichloro-6,2'-
dihydroxybiphenyl-3-yl]succinic acid 488714-16-5P,
2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-[[[2-(2-
hydroxyethoxy)ethyl]amino]carbonyl]biphenyl-3-yl]succinic acid
488714-17-6P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-4',6'-
dichloro-6,2'-dihydroxybiphenyl-3-yl]succinic acid 488714-18-7P,
2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-
[[(dimethylamino)sulfonyl]amino]biphenyl-3-yl]succinic acid
488714-19-8P, 2-[3'-Bromo-5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-
5'-chloro-6,2'-dihydroxybiphenyl-3-yl]succinic acid 488714-20-1P
, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-(4-
methylpiperazin-1-ylcarbonyl)biphenyl-3-yl]succinic acid
488714-21-2P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-

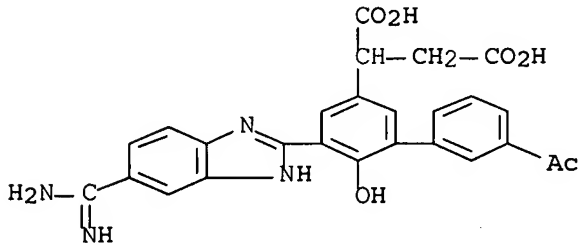
carbamimidoyl-6,2'-dihydroxybiphenyl-3-yl]succinic acid
488714-22-3P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-(((2-dimethylaminoethyl)amino)carbonyl)-6,2'-dihydroxybiphenyl-3-yl]succinic acid 488714-23-4P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-[(N'-methylureido)methyl]biphenyl-3-yl]succinic acid 488714-24-5P, Diethyl 2-[5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]succinate 488714-25-6P, 2-[5-(5-Carbamimidoyl-6-fluoro-1H-benzimidazol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]succinic acid 488714-26-7P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]-2-methylsuccinic acid 488714-27-8P, (Z)-2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-fluoro-6-hydroxy-2'-methoxybiphenyl-3-yl]but-2-enedioic acid 488714-28-9P, (Z)-2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]but-2-enedioic acid 488714-29-0P, (E)-2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]but-2-enedioic acid 488714-30-3P, 3-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]propionic acid 488714-31-4P, Methyl 3-[5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]propionate 488714-32-5P, Methyl 2-[5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]acetate 488714-33-6P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-dihydroxybiphenyl-3-yl]acetic acid 488714-34-7P, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]acetic acid 488714-35-8P, 2-[5-(5-(N-Hydroxycarbamimidoyl)-1H-benzimidazol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]succinic acid 488714-36-9P, Diethyl 2-[5-(5-(N-hydroxycarbamimidoyl)-1H-benzimidazol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]succinate 488714-37-0P, 2-[5-(5-(N-Hydroxycarbamimidoyl)-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-methylsulfonylaminobiphenyl-3-yl]succinic acid 488714-38-1P, Diethyl 2-[5-(5-(N-hydroxycarbamimidoyl)-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-ureidomethylbiphenyl-3-yl]succinate 488714-39-2P, 2-[5-(5-(N-Hydroxycarbamimidoyl)-1H-benzimidazol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]acetic acid 488714-40-5P , Diethyl 2-[5-(5-(N-hydroxycarbamimidoyl)-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-hydroxymethylbiphenyl-3-yl]succinate 488714-42-7P, Dimethyl 2-[5-(5-(N-hydroxycarbamimidoyl)-1H-benzimidazol-2-yl)-5'-aminocarbonyl-6,2'-dihydroxybiphenyl-3-yl]succinate 488714-44-9P , 2-[5-(5-(N-Hydroxycarbamimidoyl)-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-ureidomethylbiphenyl-3-yl]succinic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of [(carbamimidoyl-1H-heteroaryl)hydroxybiphenylyl]succinic acid derivs. as factor VIIa inhibitors for treating thromboembolic disorders)

RN 488713-35-5 CAPLUS

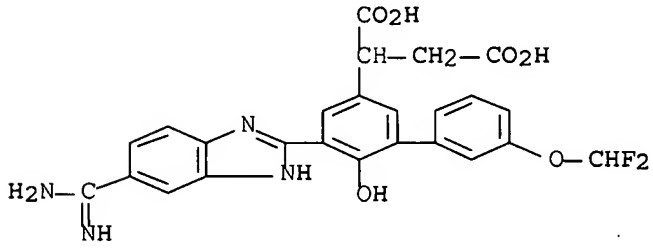
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-3'-nitro[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



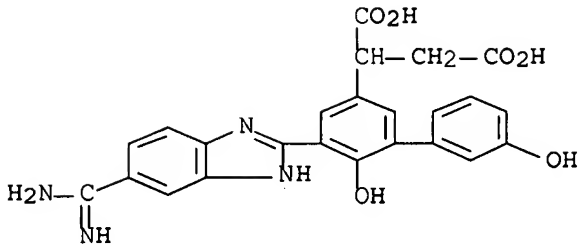
RN 488713-36-6 CAPLUS
CN Butanedioic acid, [3'-acetyl-5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



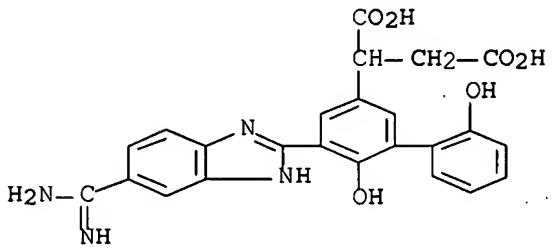
RN 488713-37-7 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-3'-(difluoromethoxy)-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



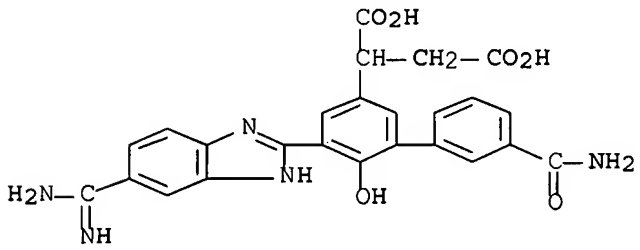
RN 488713-38-8 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-3',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



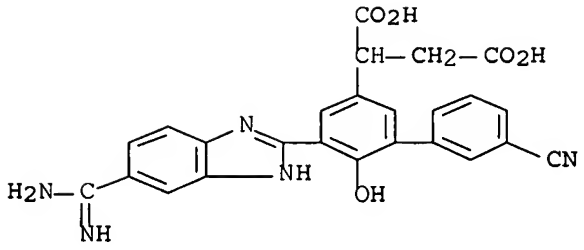
RN 488713-39-9 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



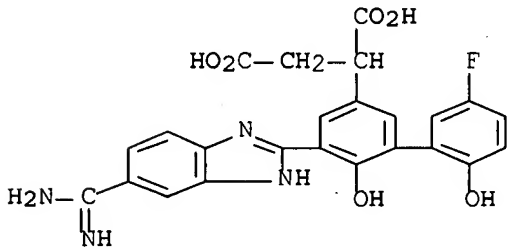
RN 488713-40-2 CAPLUS
CN Butanedioic acid, [3'-(aminocarbonyl)-5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



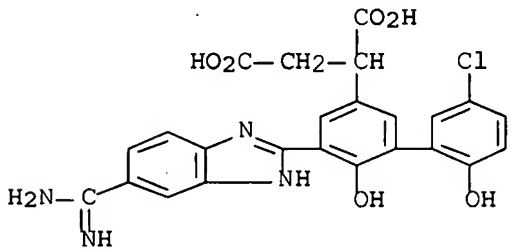
RN 488713-41-3 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-3'-cyano-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



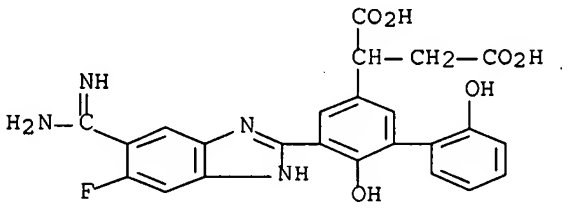
RN 488713-42-4 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



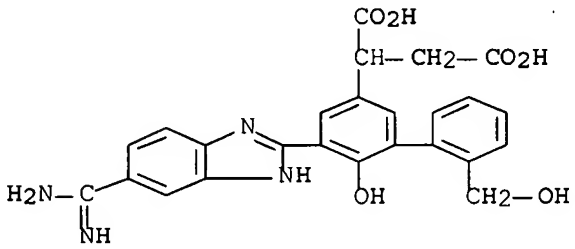
RN 488713-43-5 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-chloro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



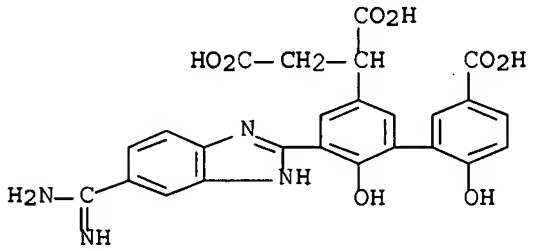
RN 488713-44-6 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-6-fluoro-1H-benzimidazol-2-yl]-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



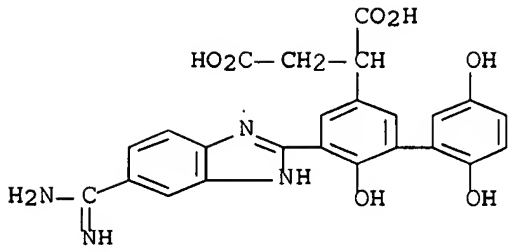
RN 488713-45-7 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-2'-(hydroxymethyl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



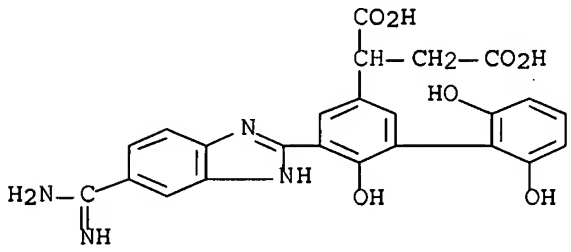
RN 488713-46-8 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-carboxy-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



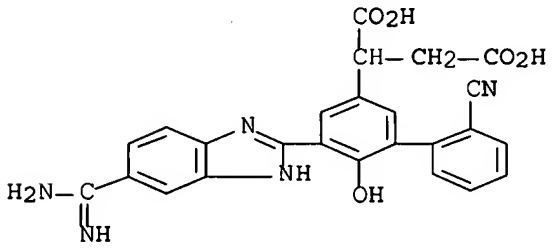
RN 488713-47-9 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',5',6-trihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



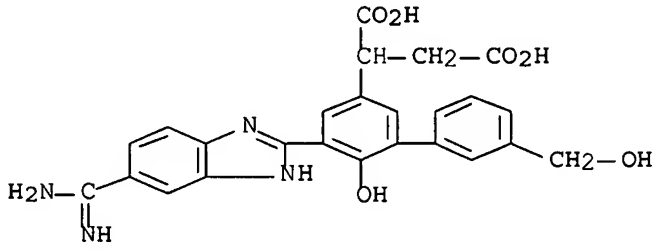
RN 488713-48-0 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6,6'-trihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



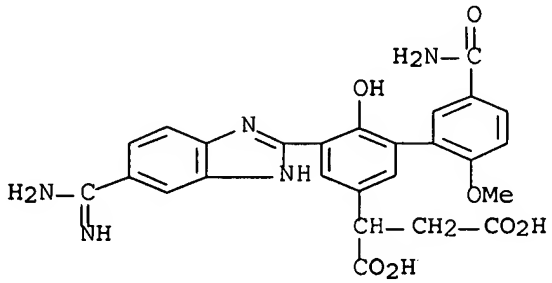
RN 488713-50-4 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2'-cyano-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



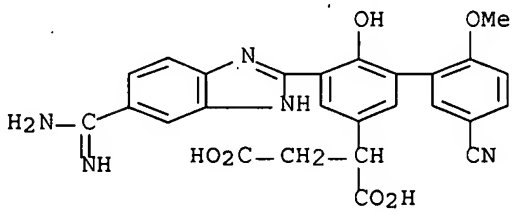
RN 488713-51-5 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-3'-(hydroxymethyl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



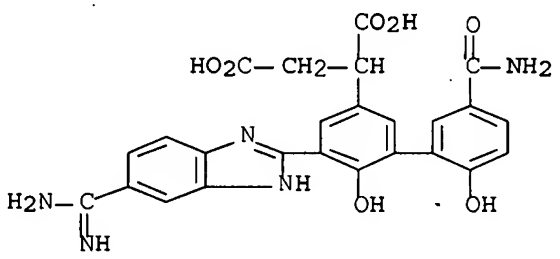
RN 488713-53-7 CAPLUS
CN Butanedioic acid, [5'-(aminocarbonyl)-5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy-2'-methoxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



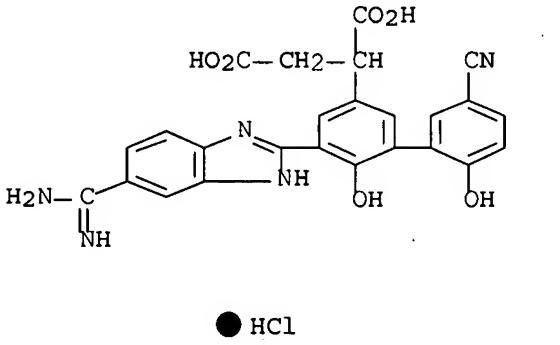
RN 488713-54-8 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-cyano-6-hydroxy-2'-methoxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



RN 488713-55-9 CAPLUS
CN Butanedioic acid, [5'-(aminocarbonyl)-5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)

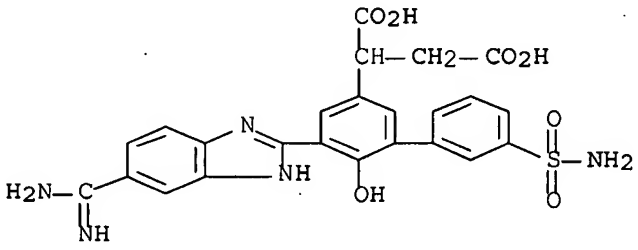


RN 488713-68-4 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-cyano-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

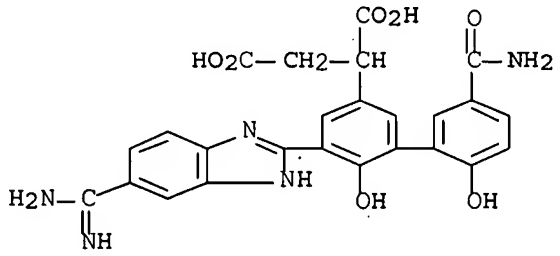


● HCl

RN 488713-69-5 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-3'-(aminosulfonyl)-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)

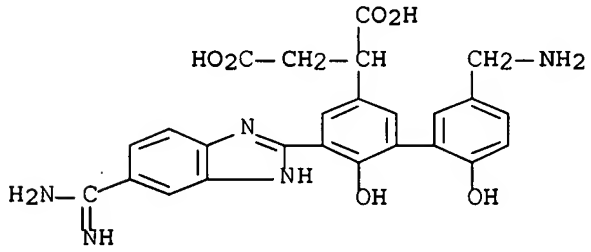


RN 488713-70-8 CAPLUS
CN Butanedioic acid, [5'-(aminocarbonyl)-5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

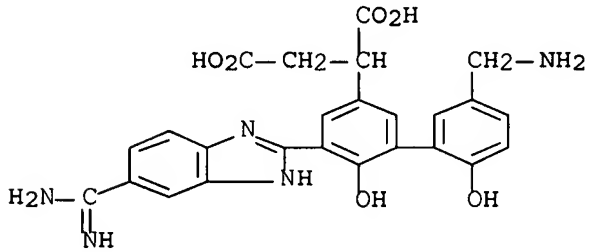


● HCl

RN 488713-71-9 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-(aminomethyl)-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)

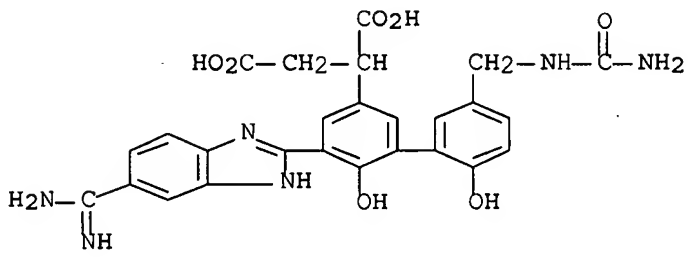


RN 488713-72-0 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-(aminomethyl)-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-, dihydrochloride (9CI) (CA INDEX NAME)

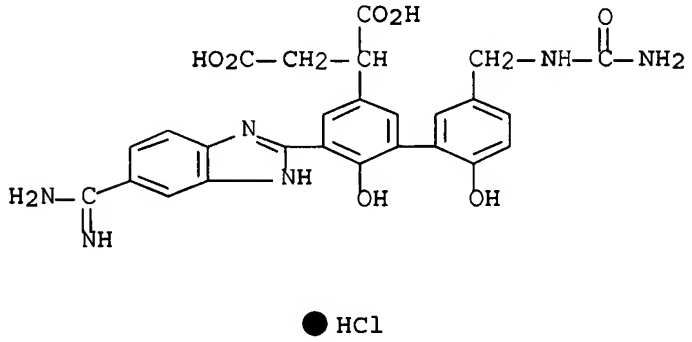


●2 HCl

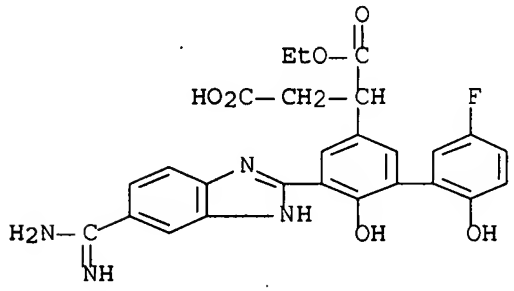
RN 488713-73-1 CAPLUS
CN Butanedioic acid, [5'-[[(aminocarbonyl)amino]methyl]-5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



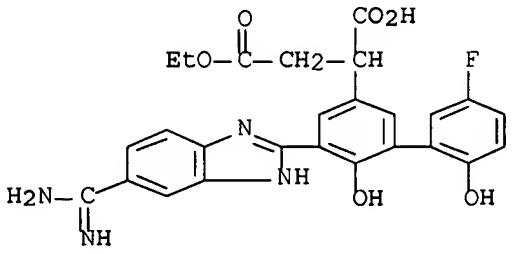
RN 488713-74-2 CAPLUS
CN Butanedioic acid, [5'-[[(aminocarbonyl)amino]methyl]-5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



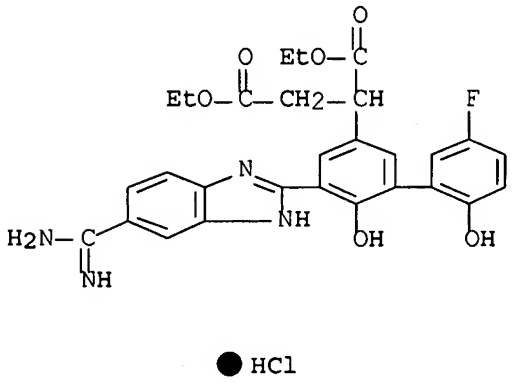
RN 488713-84-4 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-, 1-ethyl ester (9CI) (CA INDEX NAME)



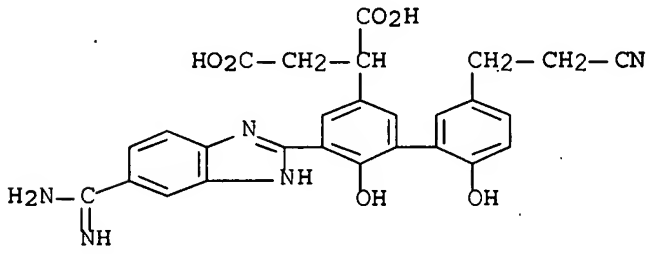
RN 488713-85-5 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-, monoethyl ester (9CI) (CA INDEX NAME)



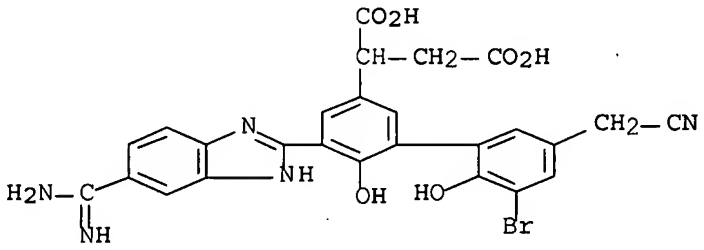
RN 488713-87-7 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-, diethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



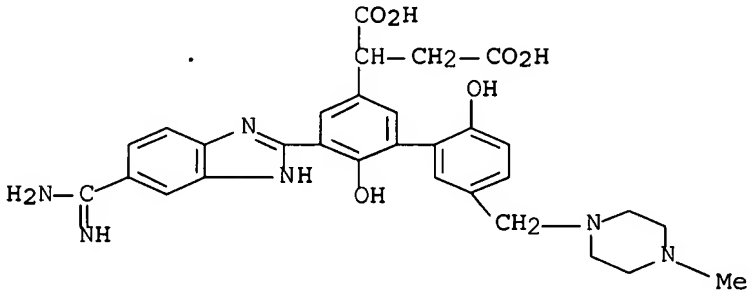
RN 488713-88-8 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-(2-cyanoethyl)-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



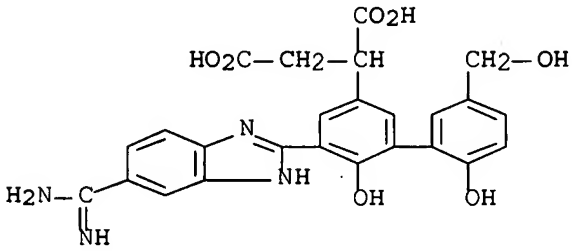
RN 488713-90-2 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-3'-bromo-5'-(cyanomethyl)-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



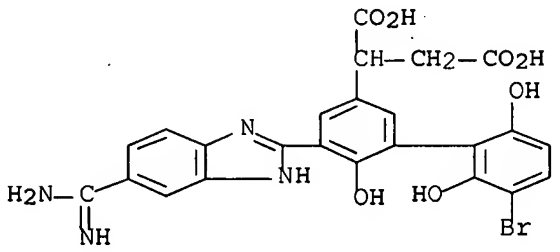
RN 488713-92-4 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy-5'-[(4-methyl-1-piperazinyl)methyl][1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



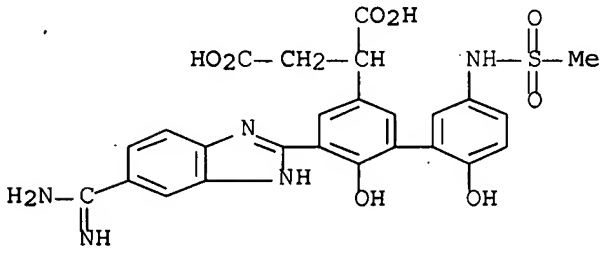
RN 488713-96-8 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy-5'-(hydroxymethyl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



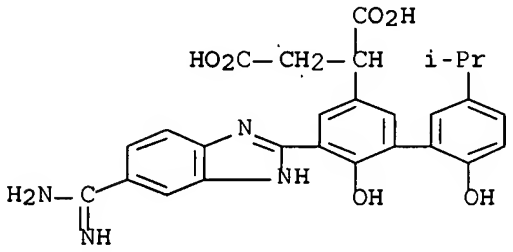
RN 488714-05-2 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-3'-bromo-2',6,6'-trihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



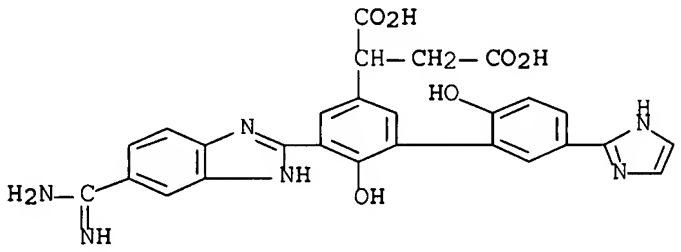
RN 488714-06-3 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy-5'-[(methylsulfonyl)amino][1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



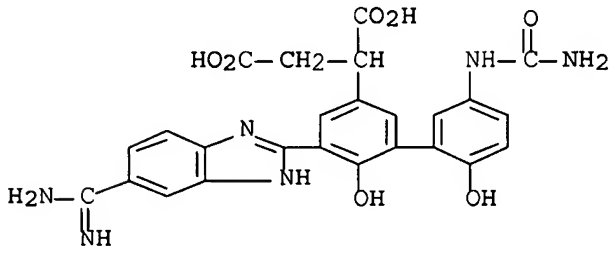
RN 488714-07-4 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy-5'-(1-methylethyl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



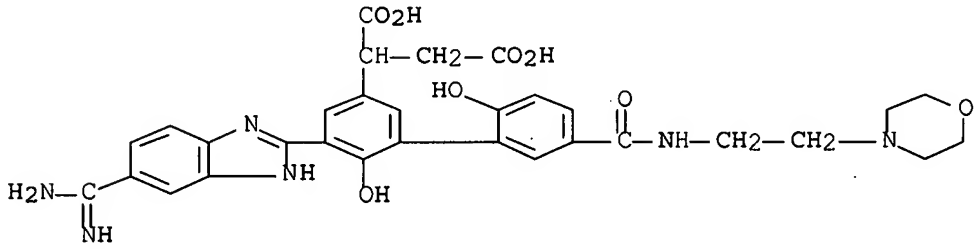
RN 488714-08-5 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy-5'-(1H-imidazol-2-yl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



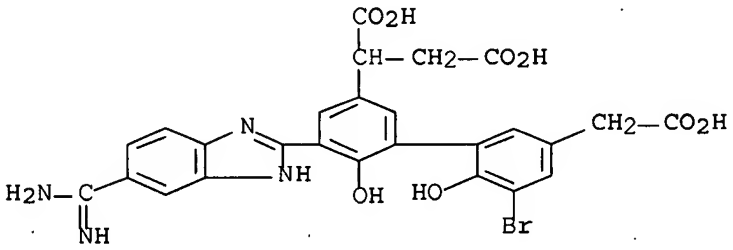
RN 488714-09-6 CAPLUS
CN Butanedioic acid, [5'-[(aminocarbonyl)amino]-5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



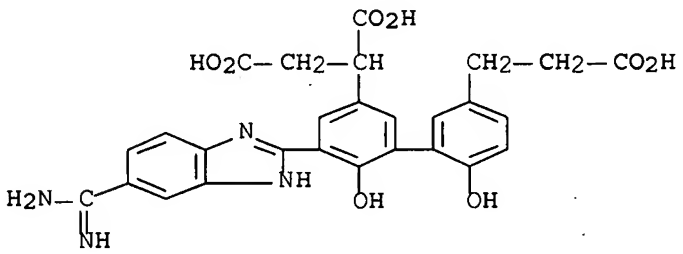
RN 488714-10-9 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy-5'-[[[2-(4-morpholinyl)ethyl]amino]carbonyl][1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



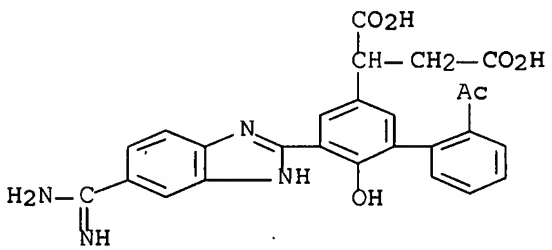
RN 488714-11-0 CAPLUS
CN [1,1'-Biphenyl]-3,3'-diacetic acid, 5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-bromo-.alpha.-(carboxymethyl)-6,6'-dihydroxy- (9CI) (CA INDEX NAME)



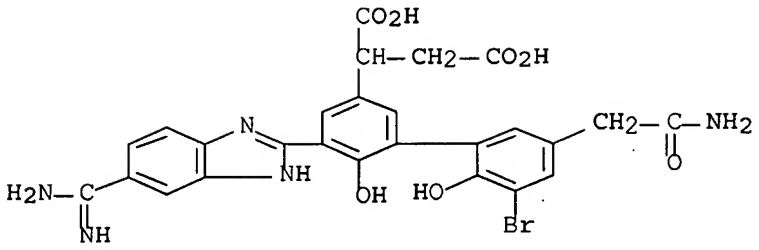
RN 488714-12-1 CAPLUS
CN [1,1'-Biphenyl]-3,3'-dipropanoic acid, 5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-.beta.-carboxy-6,6'-dihydroxy- (9CI) (CA INDEX NAME)



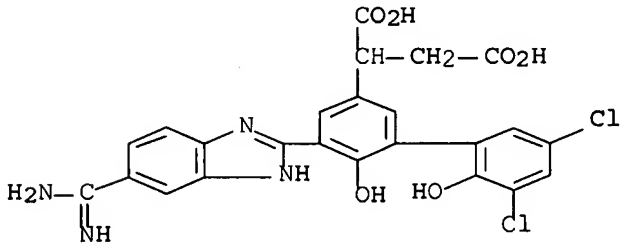
RN 488714-13-2 CAPLUS
CN Butanedioic acid, [2'-acetyl-5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



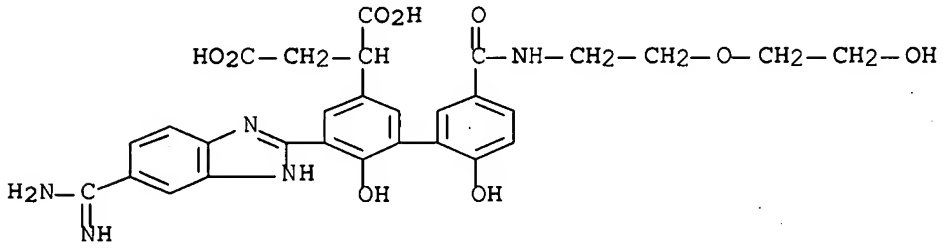
RN 488714-14-3 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-(2-amino-2-oxoethyl)-3'-bromo-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



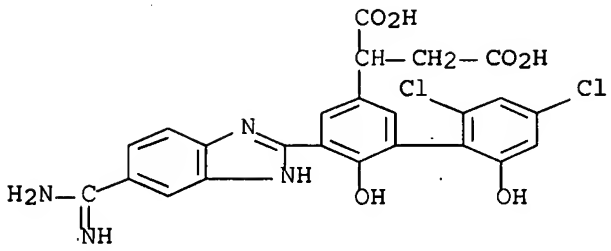
RN 488714-15-4 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-3',5'-dichloro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



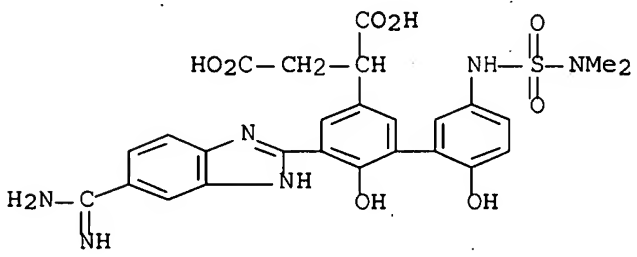
RN 488714-16-5 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy-5'-[[[2-(2-hydroxyethoxy)ethyl]amino]carbonyl][1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



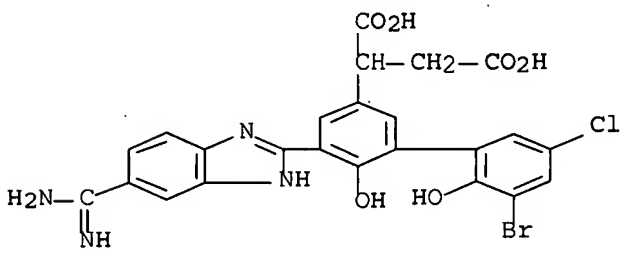
RN 488714-17-6 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',4'-dichloro-6,6'-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



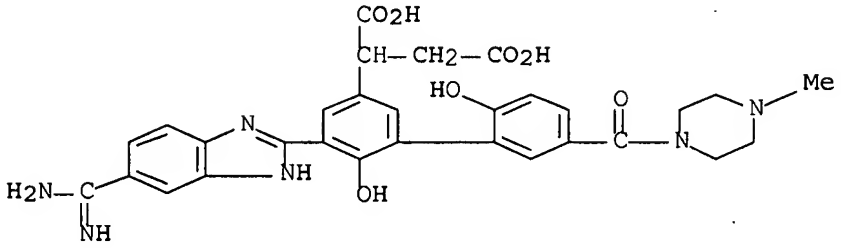
RN 488714-18-7 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-[[(dimethylamino)sulfonyl]amino]-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-(9CI) (CA INDEX NAME)



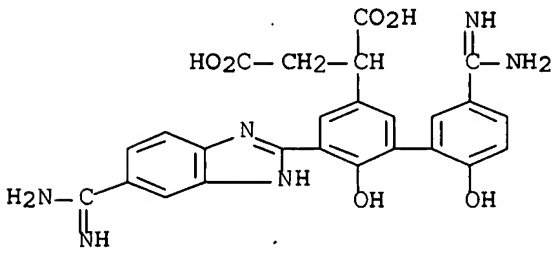
RN 488714-19-8 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-3'-bromo-5'-chloro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



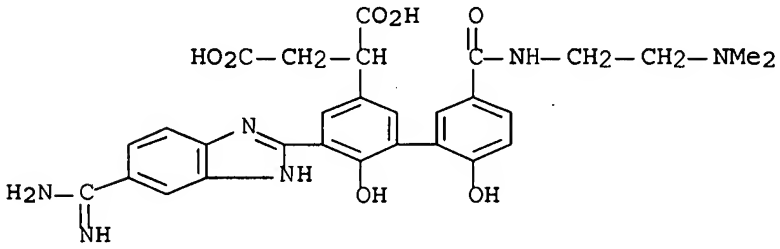
RN 488714-20-1 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy-5'-[(4-methyl-1-piperazinyl)carbonyl][1,1'-biphenyl]-3-yl]-(9CI) (CA INDEX NAME)



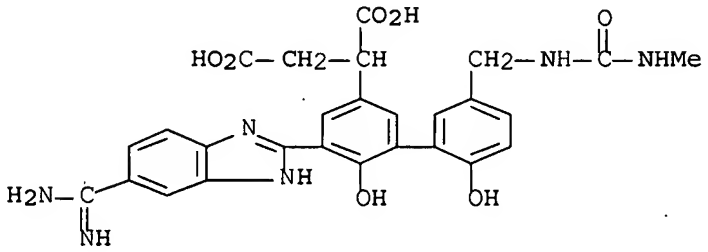
RN 488714-21-2 CAPLUS
CN Butanedioic acid, [5'-(aminoiminomethyl)-5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



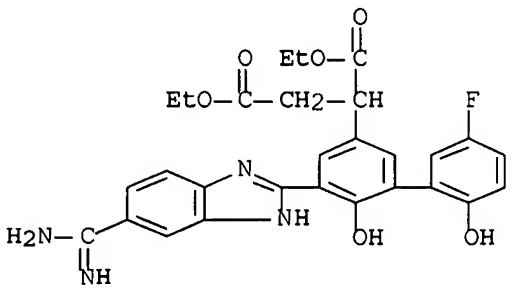
RN 488714-22-3 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-[[[2-(dimethylamino)ethyl]amino]carbonyl]-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



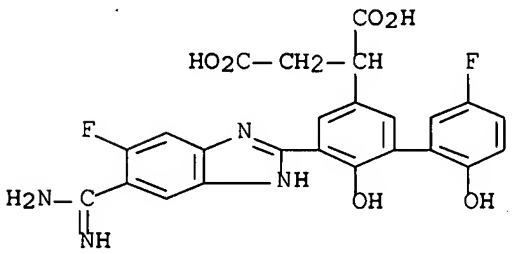
RN 488714-23-4 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy-5'-[[[(methylamino)carbonyl]amino]methyl][1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



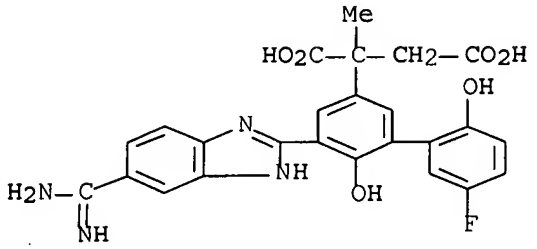
RN 488714-24-5 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 488714-25-6 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-6-fluoro-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)

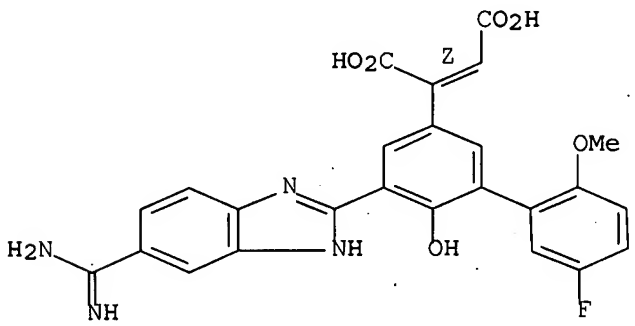


RN 488714-26-7 CAPLUS
CN Butanedioic acid, 2-[5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-2-methyl- (9CI) (CA INDEX NAME)



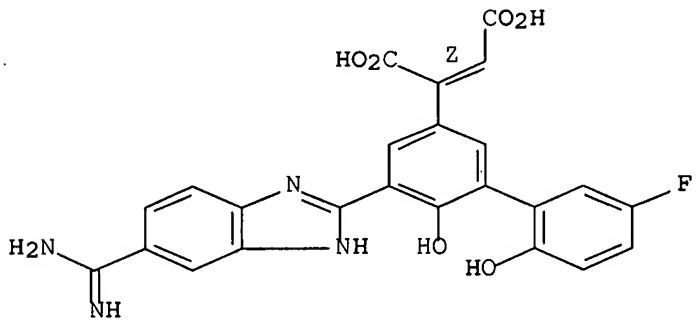
RN 488714-27-8 CAPLUS
CN 2-Butenedioic acid, 2-[5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-6-hydroxy-2'-methoxy[1,1'-biphenyl]-3-yl]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



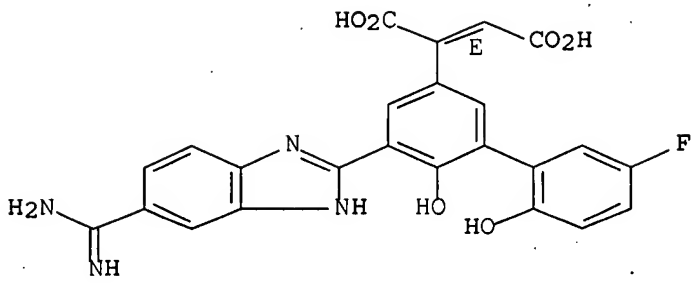
RN 488714-28-9 CAPLUS
CN 2-Butenedioic acid, 2-[5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

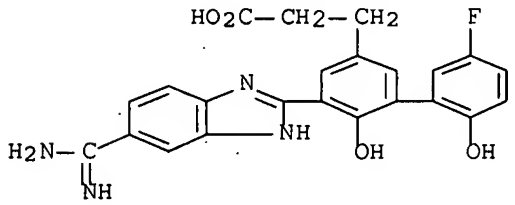


RN 488714-29-0 CAPLUS
CN 2-Butenedioic acid, 2-[5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-, (2E)- (9CI) (CA INDEX NAME)

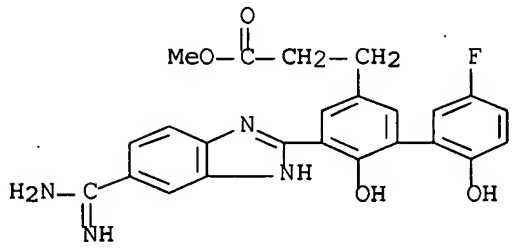
Double bond geometry as shown.



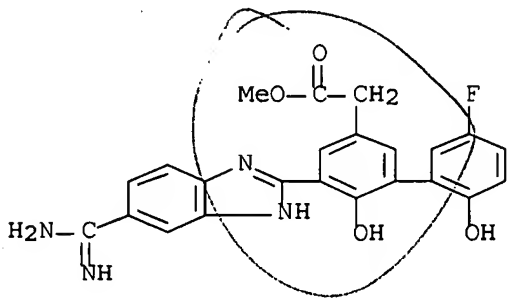
RN 488714-30-3 CAPLUS
CN [1,1'-Biphenyl]-3-propanoic acid, 5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy- (9CI) (CA INDEX NAME)



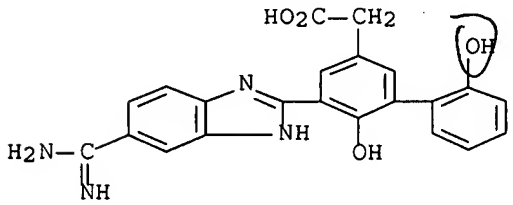
RN 488714-31-4 CAPLUS
CN [1,1'-Biphenyl]-3-propanoic acid, 5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy-, methyl ester (9CI) (CA INDEX NAME)



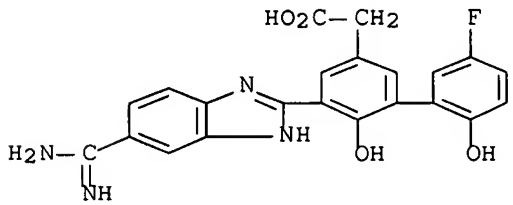
RN 488714-32-5 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy-, methyl ester (9CI) (CA INDEX NAME)



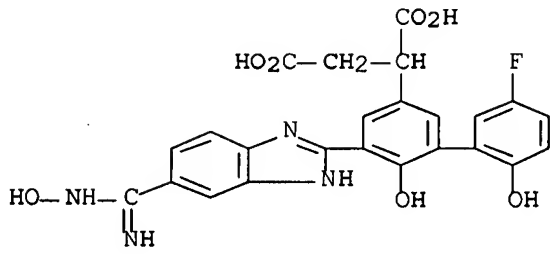
RN 488714-33-6 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy- (9CI) (CA INDEX NAME)



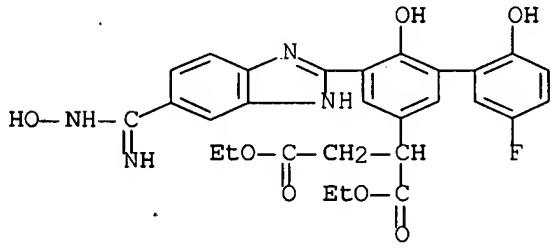
RN 488714-34-7 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy- (9CI) (CA INDEX NAME)



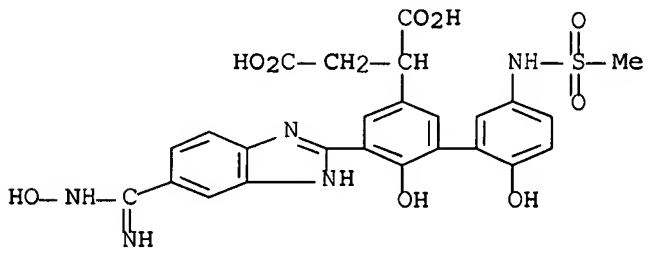
RN 488714-35-8 CAPLUS
CN Butanedioic acid, [5'-fluoro-2',6-dihydroxy-5-[5-[(hydroxyamino)iminomethyl]-1H-benzimidazol-2-yl][1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



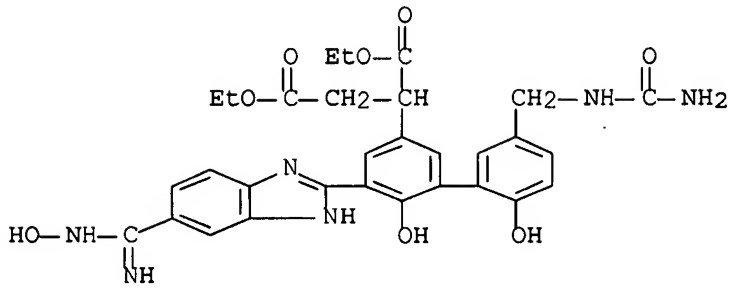
RN 488714-36-9 CAPLUS
CN Butanedioic acid, [5'-fluoro-2',6-dihydroxy-5-[5-[(hydroxyamino)iminomethyl]-1H-benzimidazol-2-yl][1,1'-biphenyl]-3-yl]-, diethyl ester (9CI) (CA INDEX NAME)



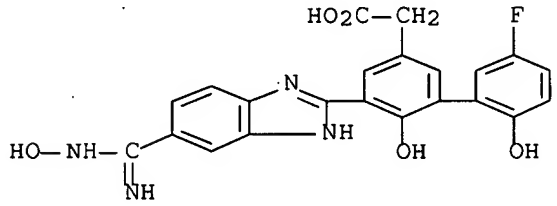
RN 488714-37-0 CAPLUS
CN Butanedioic acid, [2',6-dihydroxy-5-[5-[(hydroxyamino)iminomethyl]-1H-benzimidazol-2-yl]-5'-[(methylsulfonyl)amino][1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



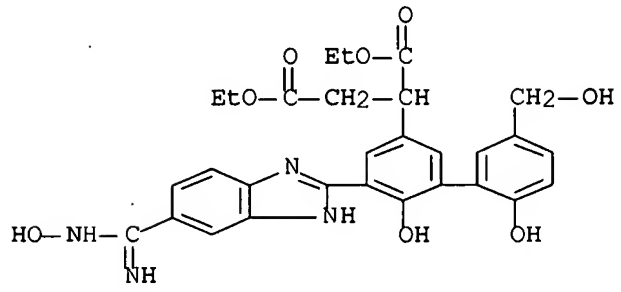
RN 488714-38-1 CAPLUS
CN Butanedioic acid, [5'-[[(aminocarbonyl)amino]methyl]-2',6-dihydroxy-5-[5-[(hydroxyamino)iminomethyl]-1H-benzimidazol-2-yl][1,1'-biphenyl]-3-yl]-, diethyl ester (9CI) (CA INDEX NAME)



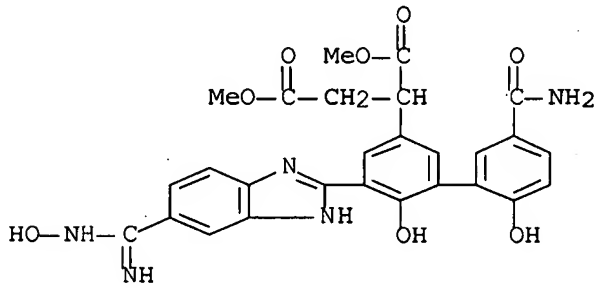
RN 488714-39-2 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5'-fluoro-2',6-dihydroxy-5-[5-[(hydroxyamino)iminomethyl]-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



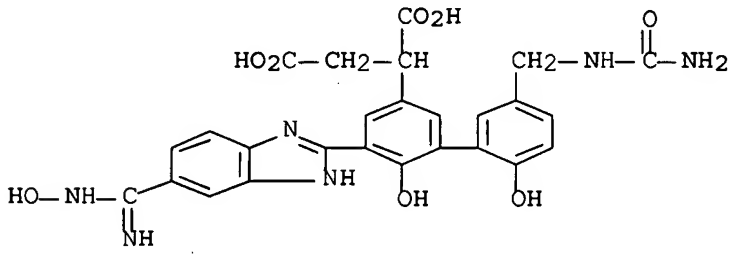
RN 488714-40-5 CAPLUS
CN Butanedioic acid, [2',6-dihydroxy-5-[5-[(hydroxyamino)iminomethyl]-1H-benzimidazol-2-yl]-5'-(hydroxymethyl)[1,1'-biphenyl]-3-yl]-, diethyl ester (9CI) (CA INDEX NAME)



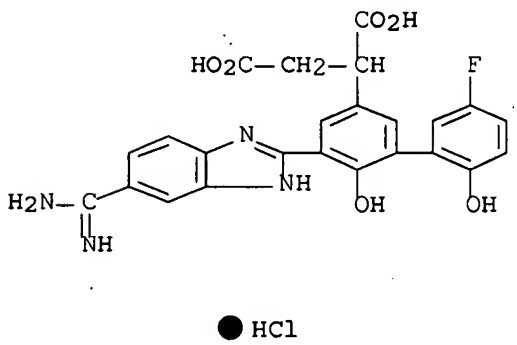
RN 488714-42-7 CAPLUS
CN Butanedioic acid, [5'-(aminocarbonyl)-2',6-dihydroxy-5-[5-[(hydroxyamino)iminomethyl]-1H-benzimidazol-2-yl][1,1'-biphenyl]-3-yl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 488714-44-9 CAPLUS
CN Butanedioic acid, [5'-[[(aminocarbonyl)amino]methyl]-2',6-dihydroxy-5-[5-[(hydroxyamino)iminomethyl]-1H-benzimidazol-2-yl][1,1'-biphenyl]-3-yl]-(9CI) (CA INDEX NAME)



IT 488713-86-6, 2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-2',6-dihydroxy-5'-fluorobiphenyl-3-yl]succinic acid monohydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of [(carbamimidoyl-1H-heteroaryl)hydroxybiphenylyl]succinic acid derivs. as factor VIIa inhibitors for treating thromboembolic disorders)
RN 488713-86-6 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-fluoro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



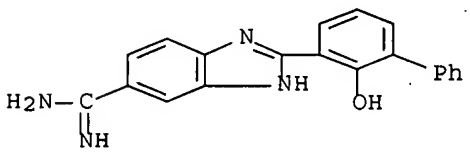
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:680206 CAPLUS Full-text
DOCUMENT NUMBER: 137:365440
TITLE: Contribution of Multicentered Short Hydrogen Bond Arrays to Potency of Active Site-Directed Serine Protease Inhibitors
AUTHOR(S): Katz, Bradley A.; Spencer, Jeffrey R.; Elrod, Kyle; Luong, Christine; Mackman, Richard L.; Rice, Mark; Sprengeler, Paul A.; Allen, Darin; Janc, James
CORPORATE SOURCE: Celera, South San Francisco, CA, 94080, USA
SOURCE: Journal of the American Chemical Society (2002), 124(39), 11657-11668
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We describe and compare the pH dependencies of the potencies and of the bound structures of two inhibitor isosteres that form multicentered short hydrogen bond arrays at the active sites of trypsin, thrombin, and urokinase type plasminogen activator (urokinase or uPA) over certain ranges of pH. Depending on the pH, short hydrogen bond arrays at the active site are mediated by two waters, one in the oxyanion hole (H2Ooxy) and one on the other (S2) side of the inhibitor (H2OS2), by one water (H2Ooxy), or by no water. The dramatic variation in the length of the active site hydrogen bonds as a function of pH, of inhibitor, and of enzyme, along with the involvement or absence of ordered water, produces a large structural manifold of active site hydrogen bond motifs. Diverse examples of multicentered and two-centered short hydrogen bond arrays, both at and away from the active site, recently discovered in several protein crystal systems, suggest that short hydrogen bonds in proteins may be more common than has been recognized. The short hydrogen bond arrays resemble one another with respect to ionic nature, highly polar environment, multitude of assocd. ordinary hydrogen bonds, and disparate pKa values of participating groups. Comparison of structures and Ki values of trypsin complexes at pH values where the multicentered short hydrogen bond arrays mediating inhibitor binding are present or absent indicate that these arrays have a minor effect on inhibitor potency. These features suggest little covalent nature within the short hydrogen bonds, despite their extraordinary shortness (as short as 2.0 .ANG.).

IT 277311-06-5D, CRA 7806, complexes with enzymes
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(multicentered short hydrogen bond arrays may contribute to potency of active site-directed serine protease inhibitors)

RN 277311-06-5 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



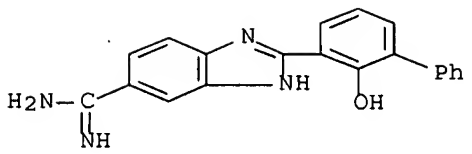
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 28 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:866569 CAPLUS Full-text
DOCUMENT NUMBER: 136:395308
TITLE: Engineering inhibitors highly selective for the S1 sites of Ser190 trypsin-like serine protease drug targets
AUTHOR(S): Katz, Bradley A.; Sprengeler, Paul A.; Luong, Christine; Verner, Erik; Elrod, Kyle; Kirtley, Matt; Janc, James; Spencer, Jeffrey R.; Breitenbucher, J. Guy; Hui, Hon; McGee, Danny; Allen, Darin; Martelli, Arnold; Mackman, Richard L.
CORPORATE SOURCE: Axys Pharmaceutical Corporation, South San Francisco, CA, 94080, USA
SOURCE: Chemistry & Biology (2001), 8(11), 1107-1121
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

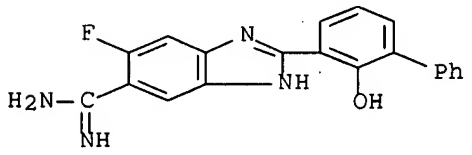
AB Background: Involved or implicated in a wide spectrum of diseases, trypsin-like serine proteases comprise well studied drug targets and anti-targets that can be subdivided into two major classes. In one class there is a serine at position 190 at the S1 site, as in urokinase type plasminogen activator (urokinase or uPA) and factor VIIa, and in the other there is an alanine at 190, as in tissue type plasminogen activator (tPA) and factor Xa. A hydrogen bond unique to Ser190 protease-arylamidine complexes between O.gamma.Ser190 and the inhibitor amidine confers an intrinsic preference for such inhibitors toward Ser190 proteases over Ala190 counterparts. Results: Based on the structural differences between the S1 sites of Ser190 and Ala190 protease-arylamidine complexes, we amplified the selectivity of amidine inhibitors toward uPA and against tPA, by factors as high as 220-fold, by incorporating a halo group ortho to the amidine of a lead inhibitor scaffold. Comparison of Ki values of such halo-substituted and parent inhibitors toward a panel of Ser190 and Ala190 proteases demonstrates pronounced selectivity of the halo analogs for Ser190 proteases over Ala190 counterparts. Crystal structures of Ser190 proteases, uPA and trypsin, and of an Ala190 counterpart, thrombin, bound by a set of ortho (halo, amidino) aryl inhibitors and of non-halo parents reveal the structural basis of the exquisite selectivity and validate the design principle. Conclusions: Remarkable selectivity enhancements of exceptionally small inhibitors are achieved toward the uPA target over the highly similar tPA anti-target through a single atom substitution on an otherwise relatively non-selective scaffold. Overall selectivities for uPA over tPA as high as 980-fold at physiol. pH were realized. The increase in selectivity results from the displacement of a single bound water mol. common to the S1 site of both the uPA target and the tPA anti-target because of the ensuing deficit in hydrogen bonding of the arylamidine inhibitor when bound in the Ala190 protease anti-target.

IT 277311-06-5, APC-7806 430476-32-7, APC 10818
430476-35-0, APC 10762
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(APC-7806 (benzimidazole) and APC-8696 (indole) series inhibitors highly selective for S1 sites of Ser190 trypsin-like serine protease drug targets and their structure-activity relationship)

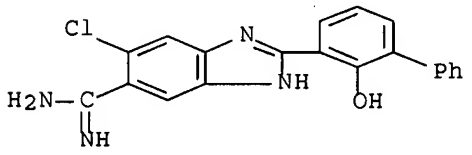
RN 277311-06-5 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



RN 430476-32-7 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 6-fluoro-2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)

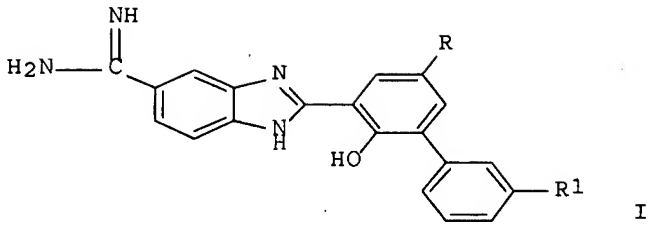


RN 430476-35-0 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 6-chloro-2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:628981 CAPLUS Full-text
DOCUMENT NUMBER: 136:47957
TITLE: Optimization of a screening lead for factor VIIa/TF
AUTHOR(S): Young, W. B.; Kolesnikov, A.; Rai, R.; Sprengeler, P. A.; Leahy, E. M.; Shrader, W. D.; Sangalang, J.; Burgess-Henry, J.; Spencer, J.; Elrod, K.; Cregar, L.
CORPORATE SOURCE: Departments of Medicinal Chemistry, Structural Chemistry, and Enzymology, Axys Pharmaceuticals, Inc., South San Francisco, CA, 94080, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(17), 2253-2256
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:47957
GI



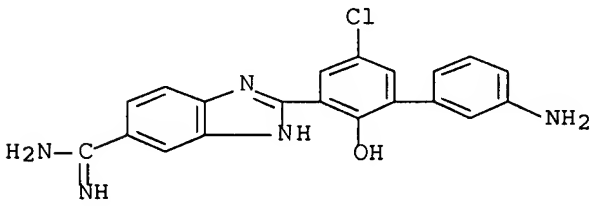
I

AB The structure-based design and progression of a screening lead (I, R = Cl, R1 = NH2) to a 3 nM factor VIIa/TF inhibitor I, (R = CH2CO2H, R1 = NO2) with improved selectivity vs. related enzymes is described.

IT 277312-01-3
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure based design of an indole biphenyl inhibitor of factor VIIa/TF with improved selectivity vs. related enzymes)

RN 277312-01-3 CAPLUS

CN 1H-Benzimidazole-5-carboximidamide, 2-(3'-amino-5-chloro-2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:500142 CAPLUS Full-text

DOCUMENT NUMBER: 135:235905

TITLE: Development of serine protease inhibitors displaying a multicentered short (<2.3 .ANG.) hydrogen bond binding mode: Inhibitors of urokinase-type plasminogen activator and factor Xa

AUTHOR(S): Verner, Erik; Katz, Bradley A.; Spencer, Jeffrey R.; Allen, Darin; Hataye, Jason; Hruzewicz, Witold; Hui, Hon C.; Kolesnikov, Aleksandr; Li, Yong; Luong, Christine; Martelli, Arnold; Radika, Kesavan; Rai, Roopa; She, Miles; Shrader, William; Sprengeler, Paul A.; Trapp, Sean; Wang, Jing; Young, Wendy B.; Mackman, Richard L.

CORPORATE SOURCE: Departments of Medicinal Chemistry Structural Biology and Biochemistry and Enzymology, Axys Pharmaceuticals Inc., South San Francisco, CA, 94080, USA

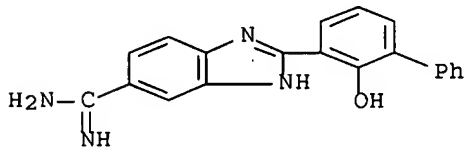
SOURCE: Journal of Medicinal Chemistry (2001), 44(17),

2753-2771
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Novel scaffolds that bind to serine proteases through a unique network of short hydrogen bonds to the catalytic Ser195 have been developed. The resulting potent serine protease inhibitors were designed from lead mol. 2-(2-hydroxyphenyl)1H-benzoimidazole-5-carboxamidine, 6b, which is known to display several modes of binding. For instance, 6b can recruit zinc and bind in a manner similar to that reported by bis(5-amidino-2- benzimidazolyl)methane (BABIM) (Nature 1998, 391, 608-612). Alternatively, 6b can bind in the absence of zinc through a multicentered network of short (<2.3 .ANG.) hydrogen bonds. The lead structure was optimized in the zinc-independent binding mode toward a panel of six human serine proteases to yield optimized inhibitors such as 2-(3-bromo-2-hydroxy-5-methylphenyl)-1H-indole-5-carboxamidine, 22a, and 2-(2-hydroxybiphenyl-3-yl)-1H-indole-5-carboxamidine, 22f. Structure-activity relationships detd. that, apart from the amidine function, an indole or benzimidazole and an ortho substituted phenol group were also essential components for optimal potency. The affinities (Ki) of 22a and 22f, for example, bearing these groups ranged from 8 to 600 nM toward a panel of six human serine proteases. High-resoln. crystal structures revealed that the binding mode of these mols. in several of the enzymes was identical to that of 6b and involved short (<2.3 .ANG.) hydrogen bonds among the inhibitor hydroxyl oxygen, Ser195, and a water mol. trapped in the oxyanion hole. In summation, novel and potent trypsin-like serine protease inhibitors possessing a unique mode of binding have been discovered.

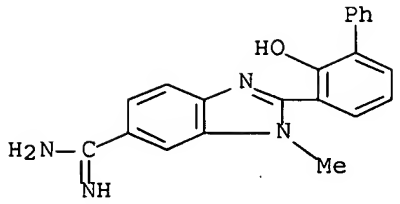
IT 277311-06-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and biol. activity of serine protease inhibitors displaying a multicentered short (<2.3 .ANG.) hydrogen bond binding mode and inhibitors of urokinase-type plasminogen activator and factor Xa)

RN 277311-06-5 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



IT 360791-74-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and biol. activity of serine protease inhibitors displaying a multicentered short (<2.3 .ANG.) hydrogen bond binding mode and inhibitors of urokinase-type plasminogen activator and factor Xa)

RN 360791-74-8 CAPLUS
CN 1H-Benzimidazole-6-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)-1-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 31 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:246441 CAPLUS Full-text
DOCUMENT NUMBER: 135:89065
TITLE: A Novel Serine Protease Inhibition Motif Involving a Multi-centered Short Hydrogen Bonding Network at the Active Site
AUTHOR(S): Katz, Bradley A.; Elrod, Kyle; Luong, Christine; Rice, Mark J.; Mackman, Richard L.; Sprengeler, Paul A.; Spencer, Jeffrey; Hataye, Jason; Janc, James; Link, John; Litvak, Joane; Rai, Roopa; Rice, Ken; Sideris, Steve; Verner, Erik; Young, Wendy
CORPORATE SOURCE: Axys Pharmaceuticals Corporation, South San Francisco, CA, 94080, USA
SOURCE: Journal of Molecular Biology (2001), 307(5), 1451-1486
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

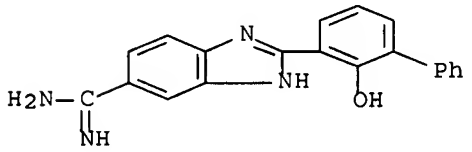
AB We describe a new serine protease inhibition motif in which binding is mediated by a cluster of very short hydrogen bonds (<2.3 .ANG.) at the active site. This protease-inhibitor binding paradigm is obsd. at high resoln. in a large set of crystal structures of trypsin, thrombin, and urokinase-type plasminogen activator (uPA) bound with a series of small mol. inhibitors (2-(2-phenol)indoles and 2-(2-phenol)benzimidazoles). In each complex there are eight enzyme-inhibitor or enzyme-water-inhibitor hydrogen bonds at the active site, three of which are very short. These short hydrogen bonds connect a triangle of oxygen atoms comprising O.gamma.Ser195, a water mol. co-bound in the oxyanion hole (H2Ooxy), and the phenolate oxygen atom of the inhibitor (O6'). Two of the other hydrogen bonds between the inhibitor and active site of the trypsin and uPA complexes become short in the thrombin counterparts, extending the three-centered short hydrogen-bonding array into a tetrahedral array of atoms (three oxygen and one nitrogen) involved in short hydrogen bonds. In the uPA complexes, the extensive hydrogen-bonding interactions at the active site prevent the inhibitor S1 amidine from forming direct hydrogen bonds with Asp189 because the S1 site is deeper in uPA than in trypsin or thrombin. Ionization equil. at the active site assocd. with inhibitor binding are probed through detn. and comparison of structures over a wide range of pH (3.5 to 11.4) of thrombin complexes and of trypsin complexes in three different crystal forms. The high-pH trypsin-inhibitor structures suggest that His57 is protonated at pH values as high as 9.5. The pH-dependent inhibition of trypsin, thrombin, uPA and factor Xa by 2-(2-phenol)benzimidazole analogs in which the pKa of the phenol group is modulated is shown to be consistent with a binding process involving ionization of both the inhibitor and the enzyme. These data further suggest that the pKa of His57 of each protease in the unbound state in soln. is about the

same,.apprx.6.8. By comparing inhibition consts. (Ki values), inhibitor solubilities, inhibitor conformational energies and corresponding structures of short and normal hydrogen bond-mediated complexes, we have estd. the contribution of the short hydrogen bond networks to inhibitor affinity (.apprx.1.7 kcal/mol). The structures and Ki values assocd. with the short hydrogen-bonding motif are compared with those corresponding to an alternate, Zn2+-mediated inhibition motif at the active site. Structural differences among apo-enzymes, enzyme-inhibitor and enzyme-inhibitor-Zn2+ complexes are discussed in the context of affinity determinants, selectivity development, and structure-based inhibitor design. (c) 2001 Academic Press.

IT 277311-06-5, APC 7806
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(novel serine protease inhibition motif involving a multi-centered short hydrogen bonding network at active site)

RN 277311-06-5 CAPLUS

CN 1H-Benzimidazole-5-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 32 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:421114 CAPLUS Full-text
DOCUMENT NUMBER: 133:58803
TITLE: Preparation of 2-arylindole- or -benzimidazolecarboxamidines and analogs as serine protease inhibitors
INVENTOR(S): Allen, Darin Arthur; Hataye, Jason M.; Hruzewicz, Witold N.; Kolesnikov, Aleksandr; Mackman, Richard Laurence; Rai, Roopa; Spencer, Jeffrey R.; Verner, Erik J.; Young, Wendy B.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035886	A2	20000622	WO 1999-US30302	19991217
WO 2000035886	A3	20001026		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,

DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2355249	A1	20000622	CA 1999-2355249		19991217
EP 1140859	A2	20011010	EP 1999-968917		19991217
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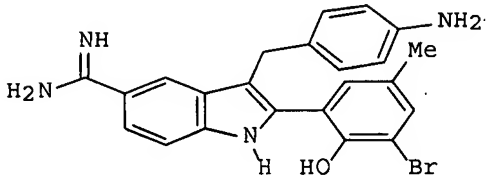
BR 9916363	A	20011211	BR 1999-16363		19991217
HU 200104987	A2	20020729	HU 2001-4987		19991217
EE 200100323	A	20020815	EE 2001-323		19991217
JP 2002532479	T	20021002	JP 2000-588148		19991217
NZ 512375	A	20031128	NZ 1999-512375		19991217
AU 779117	B2	20050106	AU 2000-27115		19991217
TR 200102533	T2	20060621	TR 2001-200102533		19991217
NO 2001002980	A	20010801	NO 2001-2980		20010615
MX 2001PA06070	A	20010911	MX 2001-PA6070		20010615
US 6867200	B1	20050315	US 2002-868276		20020118
PRIORITY APPLN. INFO.:			US 1998-113007P	P	19981218
			WO 1999-US30302	W	19991217

OTHER SOURCE(S): MARPAT 133:58803

GI



I

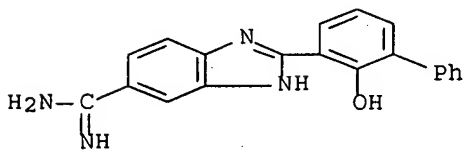
AB R1Z1Z2R2 [I; R1 = H2NC(:NH), etc.; R2 = halo, OH, CO2H, phenyl(alkyl)oxy, etc.; Z1 = (un)substituted indolylene, -benzimidazolylene, etc.; Z2 = (un)substituted phenylene, pyridinediyl, etc.] were prepd. Thus, 1-(3-bromo-2-hydroxy-5-methylphenyl)-3-(4-nitrophenyl)-1-propanone was condensed with 4-(H2NHN)C6H4C(:NH)NH2 and the product cyclized to give, after redn., title compd. II. Data for biol. activity of I were given.

IT 277311-06-5P 277311-08-7P 277311-12-3P
277311-13-4P 277311-31-6P 277311-66-7P
277311-67-8P 277311-68-9P 277311-69-0P
277311-70-3P 277312-01-3P 277312-02-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-arylindole- or -benzimidazolecarboxamidines and analogs as serine protease inhibitors)

RN 277311-06-5 CAPLUS

CN 1H-Benzimidazole-5-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)-(9CI) (CA INDEX NAME)

102b/103a



RN 277311-08-7 CAPLUS
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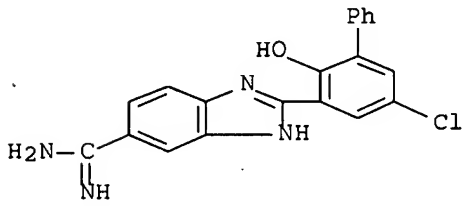

RN 277311-12-3 CAPLUS
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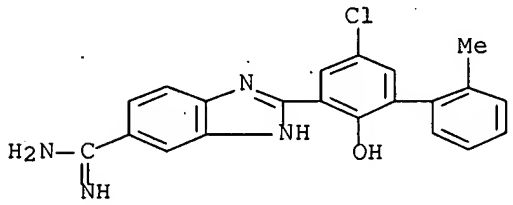
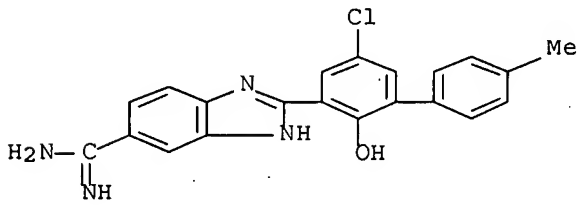


RN 277311-13-4 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-(5-chloro-2-hydroxy-4'-methyl[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



RN 277311-31-6 CAPLUS
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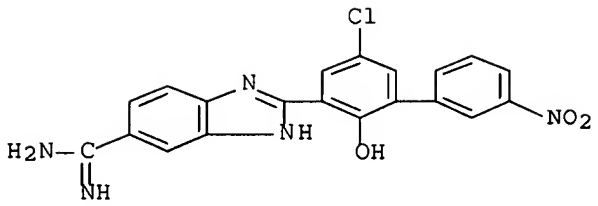

RN 277311-66-7 CAPLUS
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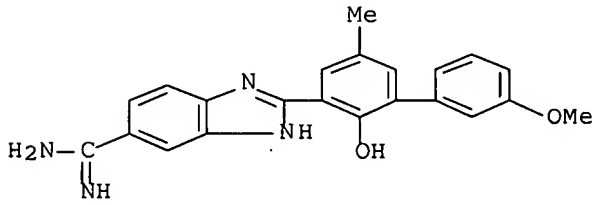

RN 277311-67-8 CAPLUS
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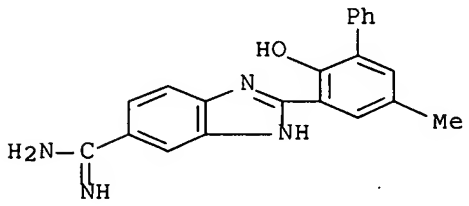

RN 277311-68-9 CAPLUS
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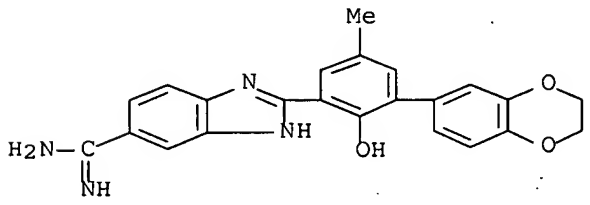

RN 277311-69-0 CAPLUS
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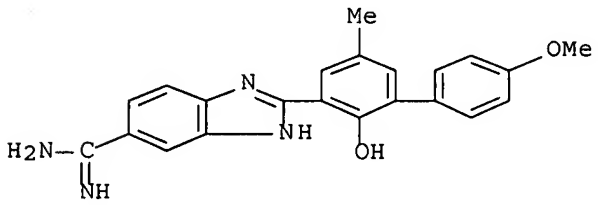
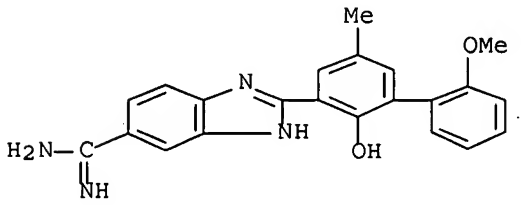


RN 277311-70-3 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-(2-hydroxy-2'-methoxy-5-methyl[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



RN 277312-01-3 CAPLUS
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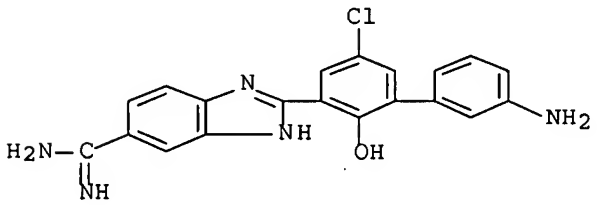
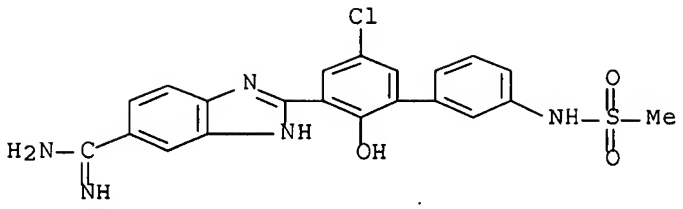


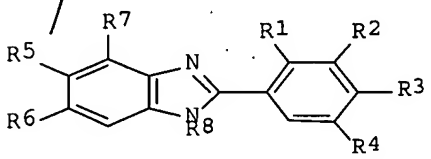
RN 277312-02-4 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-chloro-2-hydroxy-3'-[(methylsulfonyl)amino][1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



L8 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:184240 CAPLUS Full-text
DOCUMENT NUMBER: 130:209707
TITLE: Preparation of 2-substituted phenyl-benzimidazole antibacterial agents
INVENTOR(S): Ohemeng, Kwasi Adomako; Nguyen, Van Nhatton
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911627	A1	19990311	WO 1998-US18586	19980904
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 5942532	A	19990824	US 1997-924558	19970905
AU 9893054	A	19990322	AU 1998-93054	19980904
PRIORITY APPLN. INFO.:			US 1997-924558 A	19970905
			WO 1998-US18586 W	19980904

OTHER SOURCE(S): MARPAT 130:209707
GI



I

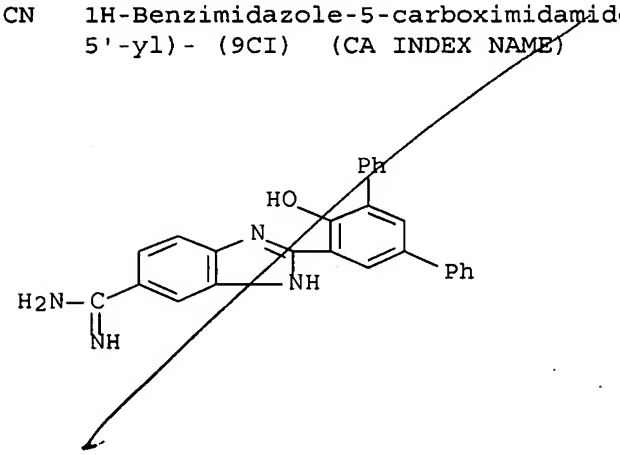
AB Benzimidazoles I [R1 = H, OH, alkoxy; R2, R3, R4 = H, OH, alkyl, CF3, halo, etc.; R5 = H, amino, amidino; R6 = nitro, C(NHR9):NR10; R7 = H, amino, nitro; R8 = H, Me], antibacterial compds., were prepd. These compds. are effective in inhibiting the action of a bacterial histidine protein kinase and are

useful as anti-infective agents against a variety of bacterial organisms, including organisms which are resistant to other known antibiotics. E.g., 3,4-diaminobenzimidate, prepd. from 3,4-diaminobenzonitrile, was treated with NH3/EtOH, then with 4-Me3CC6H4CHO to give 2-[4-(1,1-dimethylethyl)phenyl]-2H-benzimidazole-5- carboximidamide.

IT 220955-15-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of phenylbenzimidazoles as antibacterial agents)

RN 220955-15-7 CAPLUS

CN 1H-Benzimidazole-5-carboximidamide, 2-(4'-hydroxy[1,1':3',1''-terphenyl]-5'-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Executing the logoff script...

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	169.05	567.55

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-36.66	-44.46

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 14:38:42 ON 13 AUG 2007

clear of art for claim 3.

10/537,115B Yong Chu 08-14-2007

$%^STN;HighlightOn=;HighlightOff=;

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptaylc1626

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	MAY 01	New CAS web site launched
NEWS 3	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS 4	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS 5	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS 6	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS 7	MAY 21	CA/CAplus enhanced with additional kind codes for German patents
NEWS 8	MAY 22	CA/CAplus enhanced with IPC reclassification in Japanese patents
NEWS 9	JUN 27	CA/CAplus enhanced with pre-1967 CAS Registry Numbers
NEWS 10	JUN 29	STN Viewer now available
NEWS 11	JUN 29	STN Express, Version 8.2, now available
NEWS 12	JUL 02	LEMBASE coverage updated
NEWS 13	JUL 02	LMEDLINE coverage updated
NEWS 14	JUL 02	SCISEARCH enhanced with complete author names
NEWS 15	JUL 02	CHEMCATS accession numbers revised
NEWS 16	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 17	JUL 16	CAplus enhanced with French and German abstracts
NEWS 18	JUL 18	CA/CAplus patent coverage enhanced
NEWS 19	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 20	JUL 30	USGENE now available on STN
NEWS 21	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 22	AUG 06	BEILSTEIN updated with new compounds
NEWS 23	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 24	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents

NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 06:27:28 ON 14 AUG 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 06:27:49 ON 14 AUG 2007
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 13 AUG 2007 HIGHEST RN 944501-68-2
DICTIONARY FILE UPDATES: 13 AUG 2007 HIGHEST RN 944501-68-2

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http://www.cas.org/support/stngen/stndoc/properties.html

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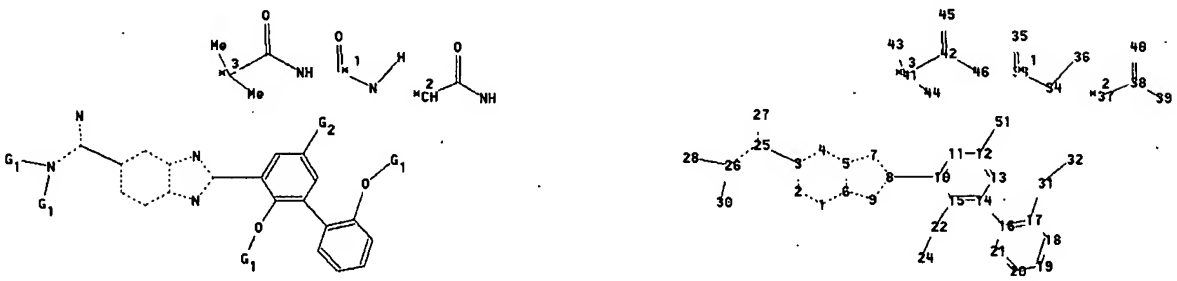

chain nodes :

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22  24  25  26  27  28  30  31  32  33  34  35  36  37  38  39  40  41  42  43  44
45  46  51
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18  19  20  21
chain bonds :
3-25  8-10  12-51  14-16  15-22  17-31  22-24  25-26  25-27  26-28  26-30  31-32
33-34  33-35  34-36  37-38  38-39  38-40  41-42  41-43  41-44  42-45  42-46
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  5-7  6-9  7-8  8-9  10-11  10-15  11-12  12-13  13-14
14-15  16-17  16-21  17-18  18-19  19-20  20-21
exact/norm bonds :
1-2  1-6  2-3  3-4  4-5  5-6  5-7  6-9  7-8  8-9  12-51  15-22  17-31  22-24  25-26
25-27  26-28  26-30  31-32  33-34  33-35  38-39  38-40  42-45  42-46
exact bonds :
3-25  8-10  14-16  34-36  37-38  41-42  41-43  41-44
normalized bonds :
10-11  10-15  11-12  12-13  13-14  14-15  16-17  16-21  17-18  18-19  19-20  20-21


G1:H,CH3,CH2,Et,n-Pr,n-Bu

G2:[*1],[*2],[*3]

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
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44:CLASS  45:CLASS  46:CLASS  51:CLASS



L1      STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1
SAMPLE SEARCH INITIATED 06:28:22 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        3 TO ITERATE

100.0% PROCESSED        3 ITERATIONS                                  2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            3 TO      163
PROJECTED ANSWERS:               2 TO      124
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L2             2 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 06:28:29 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -       73 TO ITERATE

100.0% PROCESSED       73 ITERATIONS                                 44 ANSWERS
SEARCH TIME: 00.00.01

L3            44 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     172.10     172.31

FILE 'CAPLUS' ENTERED AT 06:28:36 ON 14 AUG 2007
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FILE COVERS 1907 - 14 Aug 2007  VOL 147 ISS 8
FILE LAST UPDATED: 13 Aug 2007  (20070813/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3
L4             3 L3

=> d ibib abs tot

L4   ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2005:1330357  CAPLUS  Full-text
DOCUMENT NUMBER:          144:69827
TITLE:                    Dihydroxybiphenylacetamides as Factor VIIa inhibitors,
                          their preparation, pharmaceutical compositions, and
                          use in therapy
INVENTOR(S):              Torkelson, Steven M.; Vojkovsky, Tomas
PATENT ASSIGNEE(S):       Axys Pharmaceuticals, Inc., USA
SOURCE:                   PCT Int. Appl., 43 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005121102	A2	20051222	WO 2005-US19420		20050602
WO 2005121102	A3	20060126			

Not in national stage

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CA 2569170	A1	20051222	CA 2005-2569170		20050602
EP 1751114	A2	20070214	EP 2005-790220		20050602

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CN 1976903	A	20070606	CN 2005-80017939		20050602
IN 2006KN03600	A	20070615	IN 2006-KN3600		20061201
PRIORITY APPLN. INFO.:			US 2004-576330P	P	20040602
			WO 2005-US19420	W	20050602

OTHER SOURCE(S): CASREACT 144:69827

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a group of 12 different dihydroxybiphenylacetamides, e.g., I, which are inhibitors of Factors VIIa, IXa, Xa, and XIa, in particular Factor VIIa. The invention also relates to the prepn. of these dihydroxybiphenylacetamides, pharmaceutical compns. comprising a therapeutically effective amt. of a compd. of the invention and a pharmaceutically acceptable carrier, optionally in combination with another anticoagulant agent, as well as to the use of the compns. in the treatment of a thromboembolic disorder. C-Dimethylation of 4-methoxyphenylacetonitrile followed by acid hydrolysis, O-demethylation, esterification, formylation, and bromination gave methylpropanoate II. 3-Bromo-4-methoxybenzonitrile was converted to the corresponding boronic acid, coupled with O-methylated II, and cyclized with 3,4- diaminobenzamidine (prepn. in 3 steps from 4-amino-3-nitrobenzonitrile is given) to give dimethoxybiphenylacetate III. Compd. III underwent demethylation to the dihydroxybiphenylacetic acid followed by amidation, hydrogenation of the nitrile, acylation with (S)-2,2-dimethyl-1,3-dioxolane-4-carboxylate, and ring cleavage, resulting in the formation of I. The compds. of the invention express inhibition of Factor VIIa and Factor Xa (no data).

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2005:1314797 CAPLUS Full-text
DOCUMENT NUMBER:	144:51583
TITLE:	Preparation of benzimidazole-5-carboxamidine derivatives as factor VIIa inhibitors
INVENTOR(S):	Dickman, Daniel A.; Kumar, Dange Vijay; O'Bryan,

	Colin; Rai, Roopa; Shrader, William Dvorak
PATENT ASSIGNEE(S):	Axys Pharmaceuticals, Inc., USA
SOURCE:	PCT Int. Appl., 64 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

Not in national stage

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005118554	A2	20051215	WO 2005-US19394		20050602
WO 2005118554	A3	20060518			
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
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CA 2569163	A1	20051215	CA 2005-2569163		20050602
EP 1761504	A2	20070314	EP 2005-757137		20050602
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CN 1964951	A	20070516	CN 2005-80017896		20050602
IN 2006KN03598	A	20070615	IN 2006-KN3598		20061201
PRIORITY APPLN. INFO.:			US 2004-576382P	P	20040602
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OTHER SOURCE(S): CASREACT 144:51583; MARPAT 144:51583

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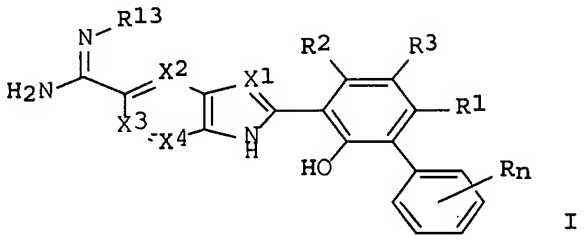

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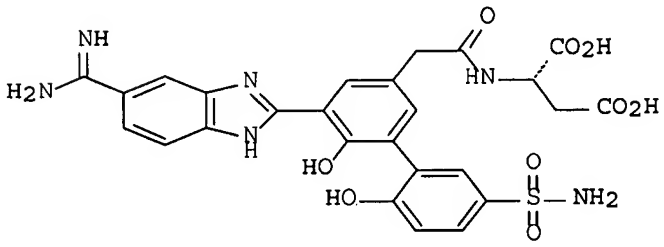

II

AB Title compds. represented by the formula I [wherein X1-X4 = independently N or CR4; R4 = H, alkyl or halo; with the proviso that not more than three of X1-X4 are -N-; R1 = H, alkyl, halo, carboxy or aminocarbonyl; R2 = H, alkyl or halo; R3 = dicarboxyalkylaminocarbonylalkyl or dicarboxyalkylaminocarbonylcycloalkyl; R = independently H, alkyl, halo, hydroxy, etc.; n = 3; R13 = H, hydroxy, alkoxy, etc.; and a zwitterion or a pharmaceutically acceptable salt thereof] were prepd. as factor VIIa inhibitors. For example, II was provided in a multi-step synthesis starting from Me 2-(4-hydroxyphenyl)acetate. I showed inhibition of Factor VIIa and Xa, and their pharmaceutical compns. were also described.

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:493686 CAPLUS Full-text
DOCUMENT NUMBER: 141:54342
TITLE: Preparation of 2-(2-hydroxybiphenyl-3-yl)-1H-benzimidazole-5-carboxamidine derivatives as factor VIIa inhibitors
INVENTOR(S): Kolesnikov, Aleksandr; Rai, Roopa; Shrader, William Dvorak; Torkelson, Steven M.; Wesson, Kieron E.; Young, Wendy B.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004050637	A2	20040617	WO 2003-US38635		20031203
WO 2004050637	A3	20040902			
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CA 2507707	A1	20040617	CA 2003-2507707		20031203
AU 2003302238	A1	20040623	AU 2003-302238		20031203
EP 1569912	A2	20050907	EP 2003-810056		20031203
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CN 1745070	A	20060308	CN 2003-80109503		20031203
JP 2006515839	T	20060608	JP 2004-557602		20031203
IN 2005KN01065	A	20060818	IN 2005-KN1065		20050603
US 2006205942	A1	20060914	US 2006-537115		20060320
PRIORITY APPLN. INFO.:			US 2002-430981P	P	20021203
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OTHER SOURCE(S): MARPAT 141:54342
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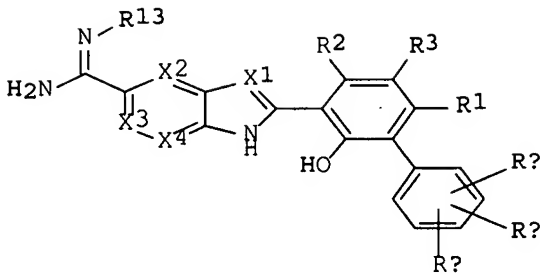

I

AB The title compds. (I) [X1-X4 = independently N or CR5 (wherein R5 = H, alkyl, or halo) with the proviso that not more than three of X1-X4 are N; R1 = H, alkyl, halo, CO2H, CONH2; R2 = H, alkyl, halo; R3 = H, halo, alkyl, alkoxy, haloalkyl, haloalkoxy, haloalkylthio, haloalkylsulfonyl, cyanoalkyl, tetrazol-5-yl, tetrazol-5-ylalkyl, hydroxyalkylcarbonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, oxalyl, NHSO2R (where R = alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl or heterocycloalkylalkyl), SO2NHCOR6 (where R6 = alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, or heterocycloalkylalkyl), SO3H, sulfonylalkyl, each N-(un)substituted CONH2, CH(CF3)NH2, or COCONH2; Rx = H, alkyl, alkylthio, halo, HO, hydroxyalkyl, alkoxy, SO2NH2, alkylaminosulfonyl, dialkylaminosulfonyl, NO2; Ry = H, alkyl, halo; Rz = H, alkyl, haloalkyl, cycloalkyl, alkylthio, halo, HO, hydroxyalkyl, nitro, cyano, alkoxy, alkoxyalkyl, alkoxyalkyloxy, hydroxyalkyloxy, aminoalkyloxy, carboxyalkyloxy, aminocarbonylalkyloxy, haloalkoxy, CO2H, etc.; R13 = H, HO, C1-10 alkoxy, COR35 (where R35 = alkyl, aryl, haloalkyl, or cyanoalkyl), CO2R36 (where R36 = alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, acyl, aryl, or haloalkyl)] and individual isomers, mixt. of isomers, or pharmaceutically acceptable salts thereof are prepd. These compds. are novel inhibitors of factors VIIa, IXa, Xa, XIa, in particular factor VIIa (no data). Pharmaceutical compns. comprising these inhibitors are useful for treating a disease in an animal mediated by factor VIIa, thromboembolic disorders, cancer or rheumatoid arthritis, in particular thromboembolic disorders. Thus, 1-tert-butyl-3-[[3'-formyl- 6,2'-bis(2-methoxyethoxymethoxy)biphenyl-3-yl]methyl]urea, 3,4-diaminobenzamidine hydrochloride, and 1,4-benzoquinone were combined in methanol, heated at 60.degree., and stirred for 2 h to give 2-[5'-(3-tert-butylureidomethyl)-2,2'-bis(2-methoxyethoxymethoxy)biphenyl- 3-yl]-1H-benzimidazole-5-carboximidamide which was dissolved in 4 M hydrogen chloride in dioxane and the soln. and stirred at room temp. for 1 h to give 2-(2,2'-dihydroxy-5'-ureidomethylbiphenyl-3-yl)-1H-benzimidazole- 5-carboximidamide hydrochloride.

=> d ibib abs hitstr 1-2

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1330357 CAPLUS Full-text
DOCUMENT NUMBER: 144:69827
TITLE: Dihydroxybiphenylacetamides as Factor VIIa inhibitors, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Torkelson, Steven M.; Vojkovsky, Tomas

PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005121102	A2	20051222	WO 2005-US19420		20050602
WO 2005121102	A3	20060126			
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IN 2006KN03600	A	20070615	IN 2006-KN3600		20061201
PRIORITY APPLN. INFO.:			US 2004-576330P	P	20040602
			WO 2005-US19420	W	20050602

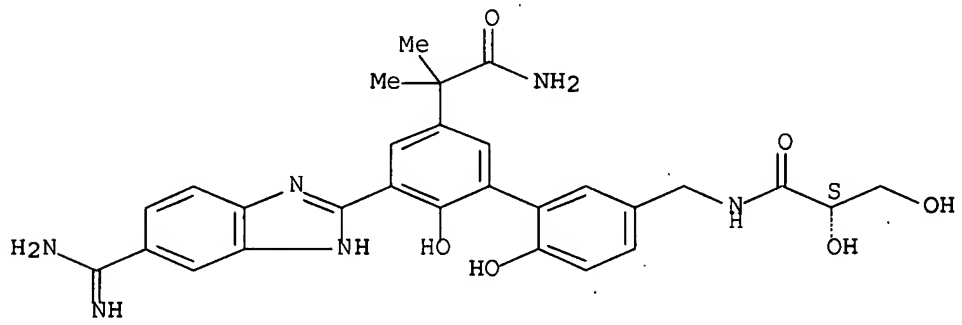
OTHER SOURCE(S): CASREACT 144:69827
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a group of 12 different dihydroxybiphenylacetamides, e.g., I, which are inhibitors of Factors VIIa, IXa, Xa, and XIa, in particular Factor VIIa. The invention also relates to the prepn. of these dihydroxybiphenylacetamides, pharmaceutical compns. comprising a therapeutically effective amt. of a compd. of the invention and a pharmaceutically acceptable carrier, optionally in combination with another anticoagulant agent, as well as to the use of the compns. in the treatment of a thromboembolic disorder. C-Dimethylation of 4-methoxyphenylacetonitrile followed by acid hydrolysis, O-demethylation, esterification, formylation, and bromination gave methylpropanoate II. 3-Bromo-4-methoxybenzonitrile was converted to the corresponding boronic acid, coupled with O-methylated II, and cyclized with 3,4- diaminobenzamidine (prepn. in 3 steps from 4-amino-3-nitrobenzonitrile is given) to give dimethoxybiphenylacetate III. Compd. III underwent demethylation to the dihydroxybiphenylacetic acid followed by amidation, hydrogenation of the nitrile, acylation with (S)-2,2-dimethyl-1,3-dioxolane-4-carboxylate, and ring cleavage, resulting in the formation of I. The compds. of the invention express inhibition of Factor VIIa and Factor Xa (no data).

IT 871822-56-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; prepn. of dihydroxybiphenylacetamides as Factor VIIa inhibitors)
RN 871822-56-9 CAPLUS
CN [1,1'-Biphenyl]-3-acetamide, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-[[[(2S)-2,3-dihydroxy-1-oxopropyl]amino]methyl]-2',6-dihydroxy-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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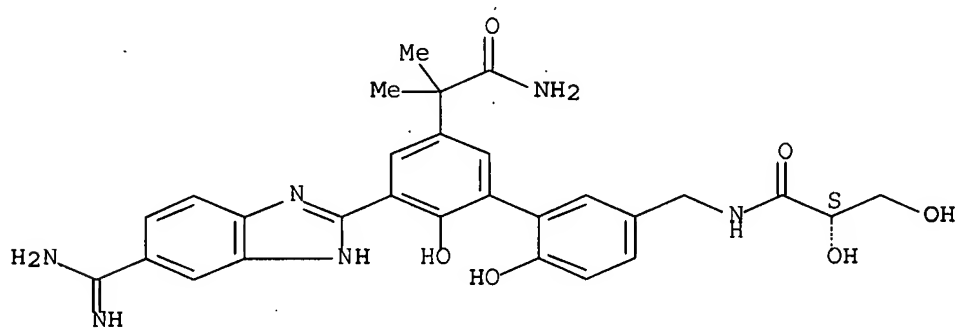
871822-62-7P 871822-64-9P 871822-65-0P
871822-66-1P 871822-67-2P 871822-68-3P
871822-69-4P 871822-70-7P 871822-72-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of dihydroxybiphenylacetamides as Factor VIIa inhibitors)
RN 871822-51-4 CAPLUS
CN [1,1'-Biphenyl]-3-acetamide, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-[[[(2S)-2,3-dihydroxy-1-oxopropyl]amino]methyl]-2',6-dihydroxy-.alpha.,.alpha.-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)

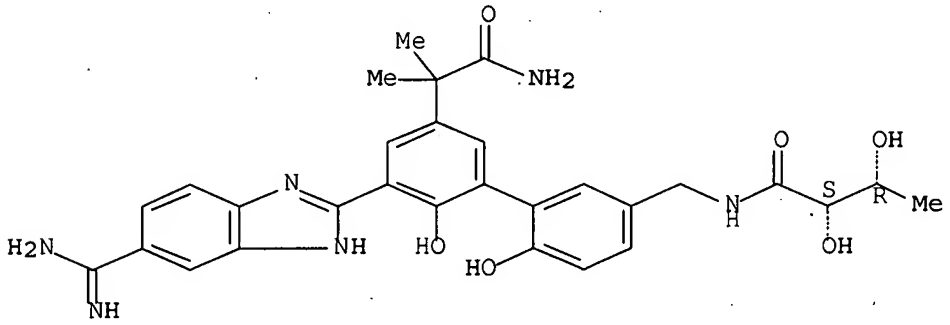
Absolute stereochemistry.



●2 HCl

RN 871822-57-0 CAPLUS
CN [1,1'-Biphenyl]-3-acetamide, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-[[[(2S,3R)-2,3-dihydroxy-1-oxobutyl]amino]methyl]-2',6-dihydroxy-.alpha.,.alpha.-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)

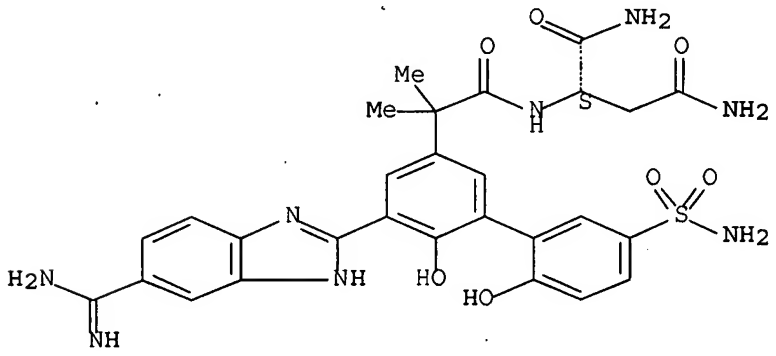
Absolute stereochemistry.



●2 HCl

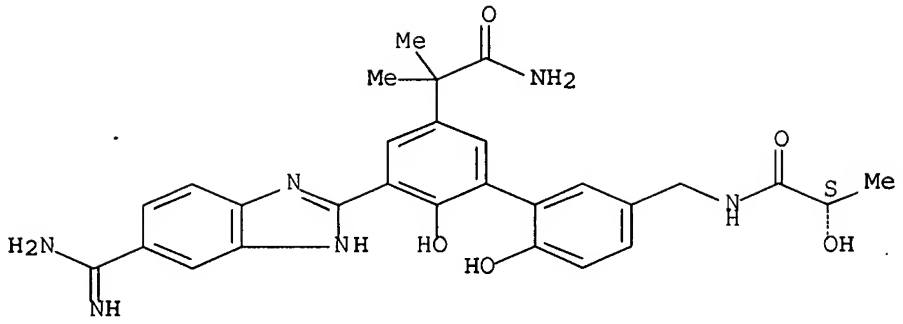
RN 871822-60-5 CAPLUS
CN Butanediamide, 2-[[2-[5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-(aminosulfonyl)-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-2-methyl-1-oxopropyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 871822-62-7 CAPLUS
CN [1,1'-Biphenyl]-3-acetamide, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy-5'-[[[(2S)-2-hydroxy-1-oxopropyl]amino]methyl]-.alpha.,.alpha.-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)

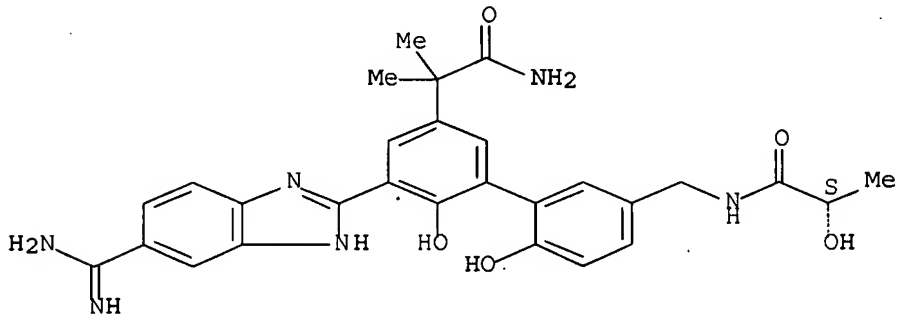
Absolute stereochemistry.



●2 HCl

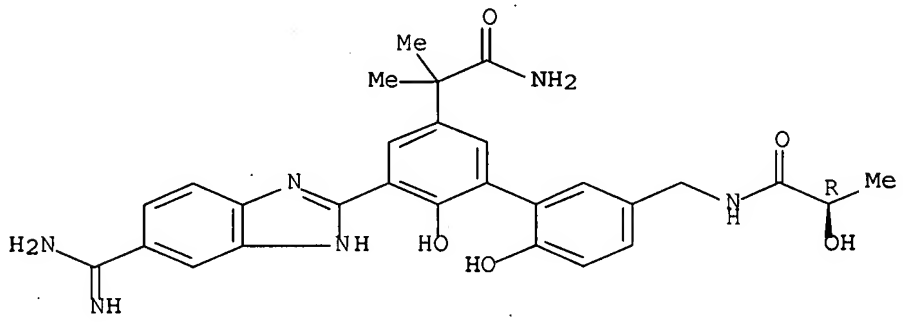
RN 871822-64-9 CAPLUS
CN [1,1'-Biphenyl]-3-acetamide, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy-5'-[[[(2S)-2-hydroxy-1-oxopropyl]amino]methyl]-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



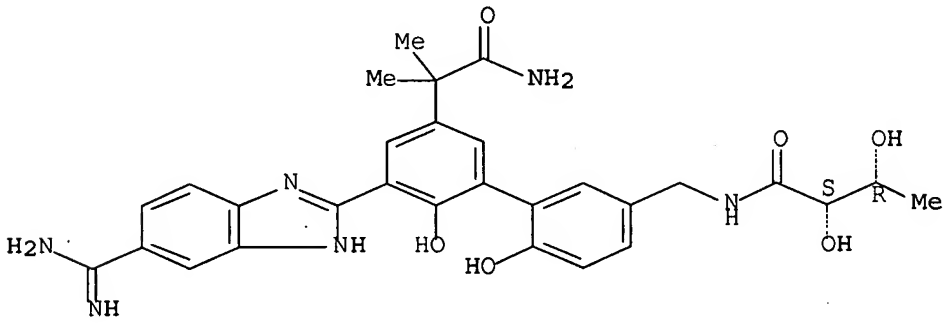
RN 871822-65-0 CAPLUS
CN [1,1'-Biphenyl]-3-acetamide, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy-5'-[[[(2R)-2-hydroxy-1-oxopropyl]amino]methyl]-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



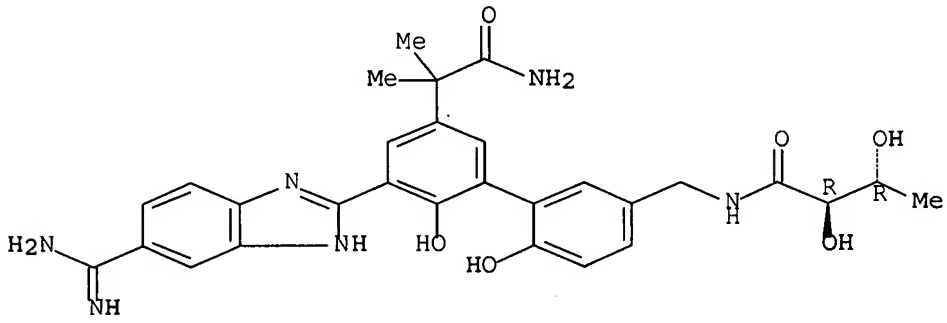
RN 871822-66-1 CAPLUS
CN [1,1'-Biphenyl]-3-acetamide, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-[[[(2S,3R)-2,3-dihydroxy-1-oxobutyl]amino]methyl]-2',6-dihydroxy-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



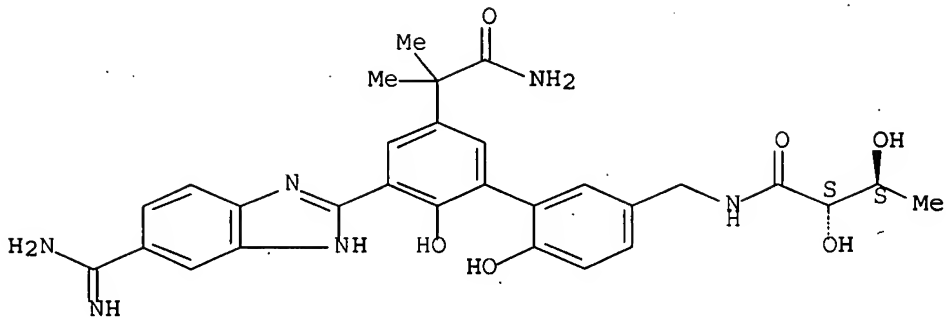
RN 871822-67-2 CAPLUS
CN [1,1'-Biphenyl]-3-acetamide, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-[[[(2R,3R)-2,3-dihydroxy-1-oxobutyl]amino]methyl]-2',6-dihydroxy-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



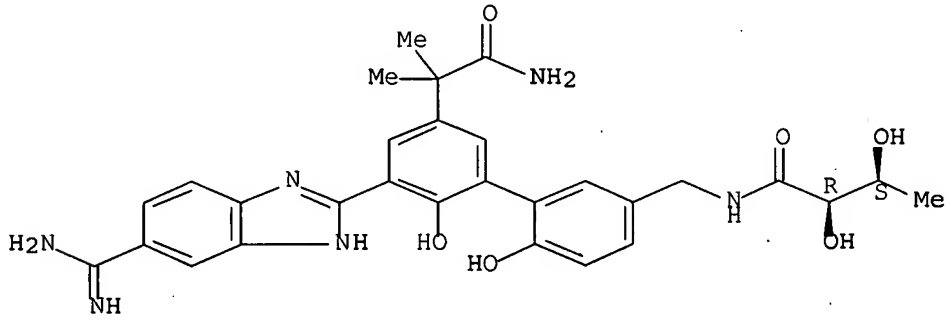
RN 871822-68-3 CAPLUS
CN [1,1'-Biphenyl]-3-acetamide, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-[[[(2S,3S)-2,3-dihydroxy-1-oxobutyl]amino]methyl]-2',6-dihydroxy-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



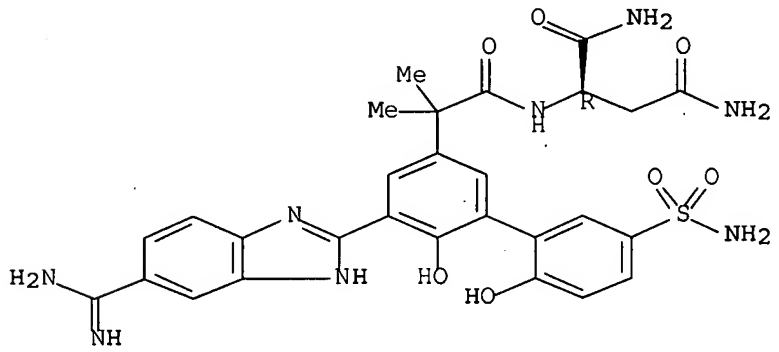
RN 871822-69-4 CAPLUS
CN [1,1'-Biphenyl]-3-acetamide, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-[[[(2R,3S)-2,3-dihydroxy-1-oxobutyl]amino]methyl]-2',6-dihydroxy-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 871822-70-7 CAPLUS
CN Butanediamide, 2-[[2-[5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-(aminosulfonyl)-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-2-methyl-1-oxopropyl]amino]-, (2R)- (9CI) (CA INDEX NAME)

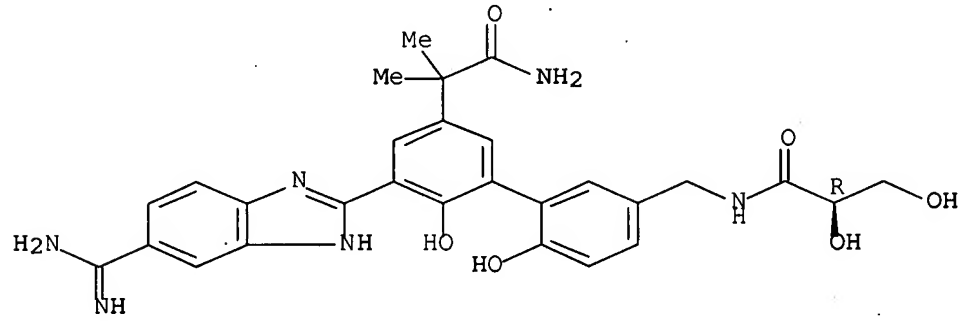
Absolute stereochemistry.



RN 871822-72-9 CAPLUS

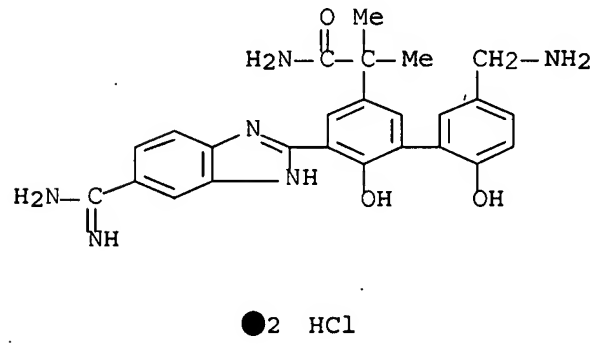
CN [1,1'-Biphenyl]-3-acetamide, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-[[[(2R)-2,3-dihydroxy-1-oxopropyl]amino]methyl]-2',6-dihydroxy-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 871822-55-8P 871822-59-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of dihydroxybiphenylacetamides as Factor VIIa inhibitors)

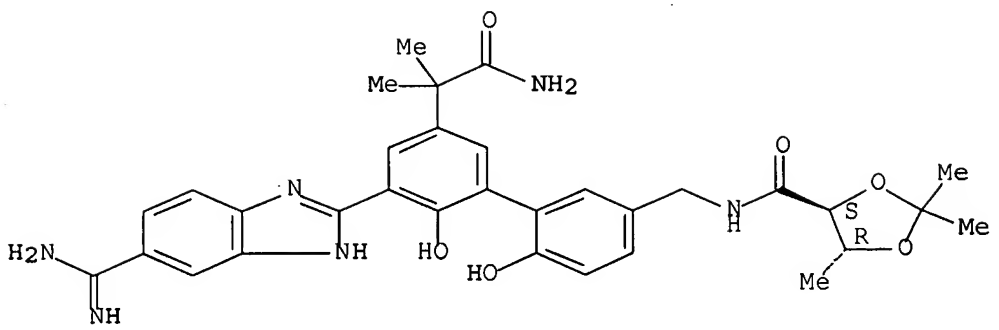
RN 871822-55-8 CAPLUS
CN [1,1'-Biphenyl]-3-acetamide, 5-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-(aminomethyl)-2',6-dihydroxy-.alpha.,.alpha.-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 871822-59-2 CAPLUS
CN 1,3-Dioxolane-4-carboxamide, N-[[5'-(2-amino-1,1-dimethyl-2-oxoethyl)-3'-[6-(aminoiminomethyl)-1H-benzimidazol-2-yl]-2',6-dihydroxy[1,1'-biphenyl]-3-yl]methyl]-2,2,5-trimethyl-, hydrochloride, (4S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



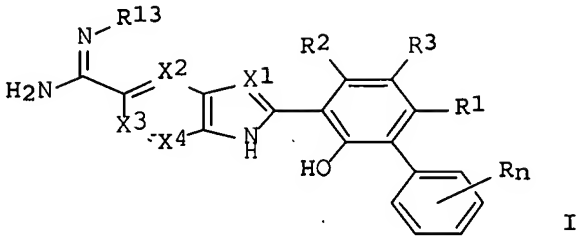
●x HCl

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1314797 CAPLUS Full-text
DOCUMENT NUMBER: 144:51583
TITLE: Preparation of benzimidazole-5-carboxamidine derivatives as factor VIIa inhibitors
INVENTOR(S): Dickman, Daniel A.; Kumar, Dange Vijay; O'Bryan, Colin; Rai, Roopa; Shrader, William Dvorak
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005118554	A2	20051215	WO 2005-US19394	20050602
WO 2005118554	A3	20060518		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005250470	A1	20051215	AU 2005-250470	20050602
CA 2569163	A1	20051215	CA 2005-2569163	20050602
EP 1761504	A2	20070314	EP 2005-757137	20050602
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1964951	A	20070516	CN 2005-80017896	20050602
IN 2006KN03598	A	20070615	IN 2006-KN3598	20061201
PRIORITY APPLN. INFO.:			US 2004-576382P	P 20040602
			WO 2005-US19394	W 20050602

OTHER SOURCE(S): CASREACT 144:51583; MARPAT 144:51583

GI



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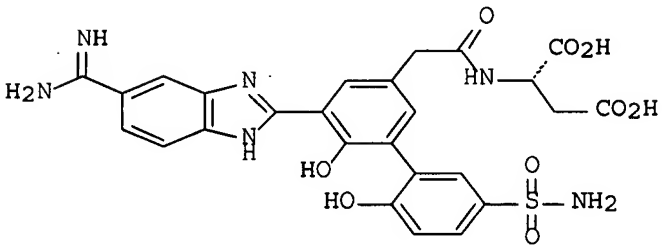


II

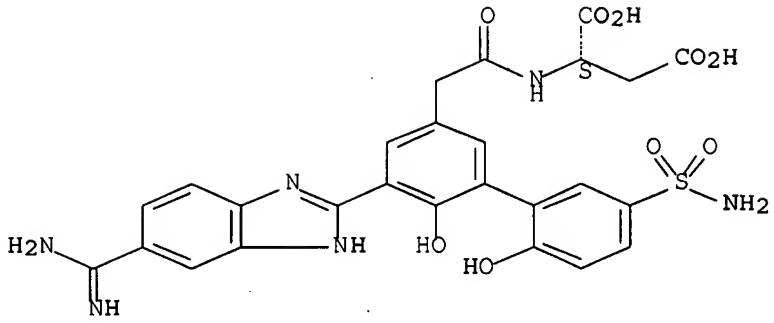
AB Title compds. represented by the formula I [wherein X1-X4 = independently N or CR4; R4 = H, alkyl or halo; with the proviso that not more than three of X1-X4 are -N-; R1 = H, alkyl, halo, carboxy or aminocarbonyl; R2 = H, alkyl or halo; R3 = dicarboxyalkylaminocarbonylalkyl or dicarboxyalkylaminocarbonylcycloalkyl; R = independently H, alkyl, halo, hydroxy, etc.; n = 3; R13 = H, hydroxy, alkoxy, etc.; and a zwitterion or a pharmaceutically acceptable salt thereof] were prepd. as factor VIIa inhibitors. For example, II was provided in a multi-step synthesis starting from Me 2-(4-hydroxyphenyl)acetate. I showed inhibition of Factor VIIa and Xa, and their pharmaceutical compns. were also described.

IT 871266-63-6P, (S)-2-[[2-[5-(5-Carbamimidoyl-1H-benzimidazol-2-yl)-6,2'-dihydroxy-5'-sulfamoylbiphenyl-3-yl]acetyl]amino]succinic acid
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of benzimidazole-5-carboxamidine derivs. as factor VIIa inhibitors)

RN 871266-63-6 CAPLUS

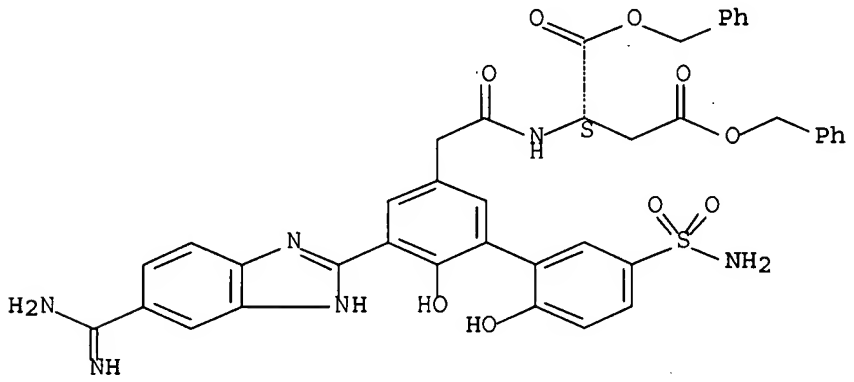
CN L-Aspartic acid, N-[[5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-(aminosulfonyl)-2',6-dihydroxy[1,1'-biphenyl]-3-yl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 871266-67-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of benzimidazole-5-carboxamidine derivs. as factor VIIa inhibitors)
RN 871266-67-0 CAPLUS
CN L-Aspartic acid, N-[[5-[5-(aminoiminomethyl)-1H-benzimidazol-2-yl]-5'-(aminosulfonyl)-2',6-dihydroxy[1,1'-biphenyl]-3-yl]acetyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	20.91	193.22

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION

CA SUBSCRIBER PRICE -3.90 -3.90

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 06:30:55 ON 14 AUG 2007